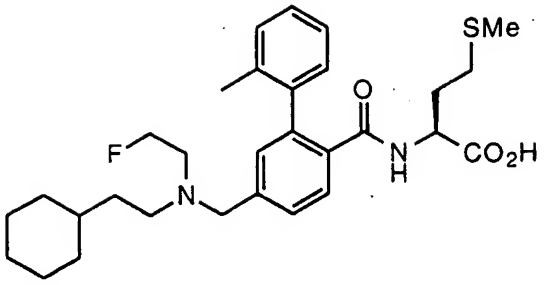
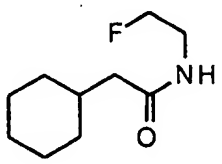
MS m/z 385 (M^+ - 1, 100).



Example 1094

N-[4-(N-(2-cyclohexylethyl)-N-2-fluoroethylaminomethyl)-2-(2-methylphenyl)benzoyl]methionine

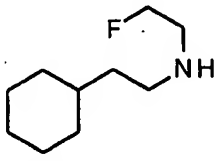


Example 1094A

N-(2-Fluoroethyl)-2-cyclohexylacetamide

Following the procedure of example 1178E, 2-fluoroethylamine•HCl (1.00 g, 10.00 mmol) provided 1.58 g (84%) of the title compound.

MS (DCI, NH_3): 188 (MH^+).

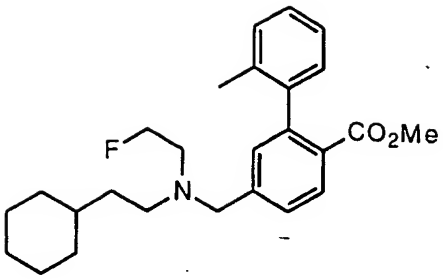


Example 1094B

N-(2-Fluoroethyl)-N-2-cyclohexylethylamine

Following the procedure of example 1178F, example 1094A (1.54 g, 8.2 mmol) provided 1.30 g (92%) of the title compound.

MS (DCI, NH_3): 172 (MH^+).

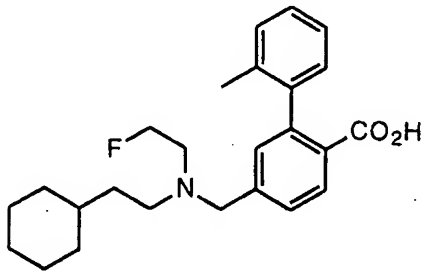


Example 1094C

N-[4-(N-(2-cyclohexylethyl)-N-2-fluoroethylaminomethyl)-2-(2-methylphenyl)benzoic acid methyl ester

Following the procedure of example 1178G and substituting potassium phosphate for diisopropylethylamine, and heating at 60°C for 60 hours, example 1094B (188 mg, 1.10 mmol) provided 288 mg (70%) of the title compound.

MS (ESI +): 410 ($M + NH_4^+ - F^-$).

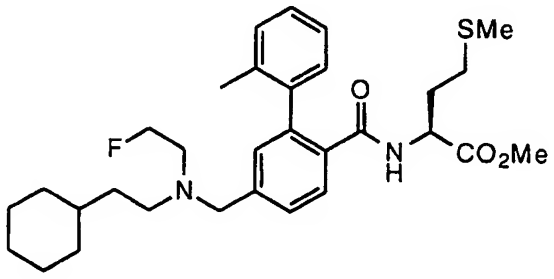


Example 1094D

N-[4-(N-(2-cyclohexylethyl)-N-2-fluoroethylaminomethyl)-2-(2-methylphenyl)benzoic acid

Following the procedure of example 1178H, example 1094C (0.28 g, 0.68 mmol) provided 0.25 g (93%) of the title compound.

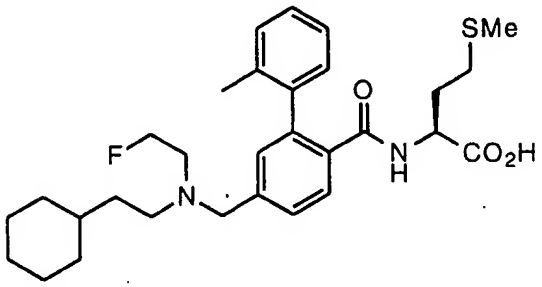
MS (DCI, NH_3): 398 (MH^+).



Example 1094E

N-[4-(N-(2-cyclohexylethyl)-N-2-fluoroethylaminomethyl)-2-(2-methylphenyl)benzoyl]methionine, methyl ester

Following the procedure of example 1178 I, example 1094D (245 mg, 0.62 mmol) provided 257 mg (77%) of the title compound. MS: (ESI+): 541 $(MH)^+$: (ESI-); 539 (M-H).



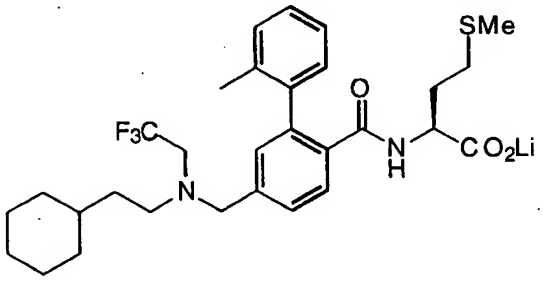
12020

Example 1094F

N-[4-(N-(2-cyclohexylethyl)-N-2-fluoroethylaminomethyl)-2-(2-methylphenyl)benzoyl]methionine

Following the procedure of example 1104D, example 1094E (250 mg, 0.46 mmol) provided 240 mg of the title compound.

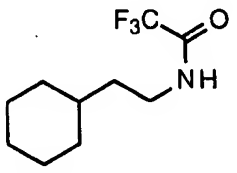
12025 ^1H NMR (δ ,$CDCl_3$): 7.75 (2H), 7.0-7.4 (4H), 6.4 (1H), 3.8-4.6 (9H), 2.9-3.3 (4H), 0.8-2.3 (21H). MS: (ESI+): 527 $(MH)^+$: (ESI-); 525 (M-H). Calc'd for $C_{30}H_{41}FN_2O_3S \cdot 0.90H_2O$: C 66.12 H 7.92 N 5.14; Found: C 66.13 H 7.77 N 4.86.



12030

Example 1103

N-[4-(N-(2-cyclohexylethyl)-N-2,2,2-trifluoroethylaminomethyl)-2-(2-methylphenyl)benzoyl]methionine, lithium salt



12035

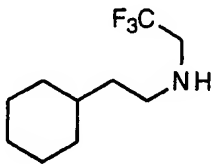
Example 1103A

N-trifluoroacetyl-2-cyclohexylethyl amide

Cyclohexylethyamine (1.27 g, 10 mmol) was dissolved in 10 mL of methylene chloride and pyridine (1.8 mL, 15.0 mol) was added and the mixture cooled to -10° C in an

ice/acetone bath. The solution was treated with trifluoroacetic anhydride (1.7 mL, 12.0 mmol) in 5 mL of methylene chloride dropwise. After stirring for 2 hours at 0°C the mixture was diluted with 100 mL of ether and extracted with water, 1M aqueous phosphoric acid and satureaed aqueous sodium bicarbonate, dried, filtered and concentrated to give a white solid (2.07g, 92%).

MS (DCI, NH_3): 241 $(M+NH_4)^+$.

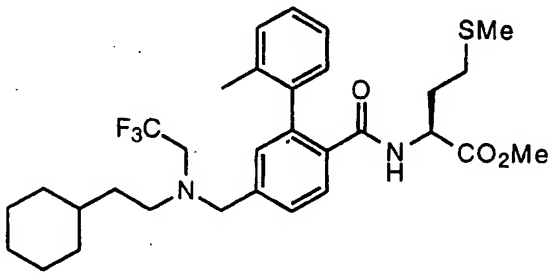


Example 1103B

N-2-trifluoroethyl-2-cyclohexylethyl amine

A solution of lithium aluminum hdydride (9 mL of a 1M solution in THF, 9 mmol) was added to a solution of example 1103A (0.67 g, 3.0 mmol) and the mixture was heated to reflux for 2 hours and then cooled to room temperature. The reaction was quenched by the same procedure as example 1178F to provide 0.58 g (92%) of the title compound.

MS (DCI, NH_3): 228 $(M+NH_4)^+$.



Example 1103C

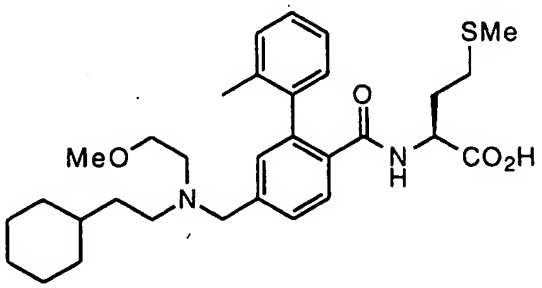
N-[4-(N-(2-cyclohexylethyl)-N-2,2,2-trifluoroethylaminomethyl)-2-(2-methylphenyl)benzoyl]methionine methyl ester

A solution of example 1103B (210 mg, 1.0 mmol) and the aldehyde from example 403G (192 mg, 0.5 mmol) in 3 mL of 1,2 dichoroethane was treated with acetic acid (0.14 mL, 2.5 mmol) and the mixture stirred for 10 minutes. The mixture was treated with sodium triacetoxyborohydride (213 mg, 1.0 mmol) and the mixture stirred overnight. The work-up was the same as that of example 1134E. The crude product was purified by chromatography on silica gel (20 g, 20% ethyl acetate/hexanes) to provide 96 mg (33%) of the title compound.

^1H NMR (300 MHz., $CDCl_3$): δ 7.91, dd, 1H; 7.42, dd, 1H; 7.18 - 7.36, m, 4H; 7.15, bs, 1H; 5.88, bd, 1H' 4.63, m, 1H; 3.83, s, 2H; 3.65, s, 3H; 3.09, q, 2H; 2.64, t, 2H; 2.18,

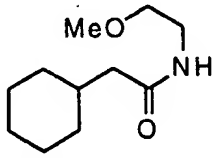
s, 1.5 H (o-tolyl); 2.07, s, 1.5H (o-tolyl); 2.05, m, 1H; 2.03, s, 1.5H (MeS); 2.01, s, 1.5H (MeS); 1.87, m, 1H; 1.61, bm, 6H; 1.35, m, 2H; 1.20, m 2H; 1.14, m, 2H; 0.85, m, 2H.
MS (ESI+): 579 (MH+): (ESI-): 577 (M-H).

Prepared according to the procedure of example 1178J.
^{1}H NMR (300 MHz., dmso d6): δ 7.52, d, 1H; 7.35, d, 1H; 7.23, m, 3H; 7.12, m, 3H; 6.91, d, 1H; 3.81, s, 2H; 3.66, m, 1H; 3.38, q, 2H; 2.56, t, 2H; 2.06, m, 1H; 2.00, bs, 3H; 1.92, s, 3H; 1.58, m, 7H; 1.00 - 1,38, m, 6H; 0.80, m, 2H.
MS (ESI+): 587; 571; 565 (MH+): (ESI-): 563 (M-H). Calc'd for $C_{30}H_{38}LiN_2O_3S \cdot 1.75 H_2O$; C 59.84; H 6.95; N 4.65; Found: C 59.86; H 6.57; N 4.45.



Example 1104

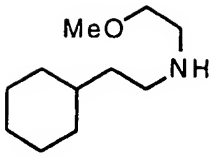
N-[4-(N-(2-cyclohexylethyl)-N-2-methoxyethylaminomethyl)-2-(2-methylphenyl)benzoyl]methionine



Example 1104A

N-(2-methoxyethyl)-2-cyclohexylacetamide

The acid chloride from example 1178E (1.60 g, 10 mmol) in 10 mL of methylene chloride was added dropwise to a cold (0°C) solution of 2-methoxyethylamine (1.3 mL, 15 mmol) and pyridine (1.9 mL, 22 mmol) in 10 mL of methylene chloride and the mixture was stirred overnight. The mixture was diluted with ethyl ether and washed with water, 1M aqueous phosphoric acid , 2M aqueous sodium carbonate and brine, dried, filtered and concentrated to provide 1.70 g (85%) of the title compound as a white solid.
^{1}H NMR (300 MHz., $CDCl_3$): δ 5.89, bs, 1H; 3.46, m, 4H; 3.37, s, 3H; 2.05, d, 2H; 1.79, m, 1H; 1.70, bm, 6H; 1.24, m, 2H; 1.17, m, 1H; 0.95, m, 2H.
MS (DCI, NH_3): 200 (MH^+).

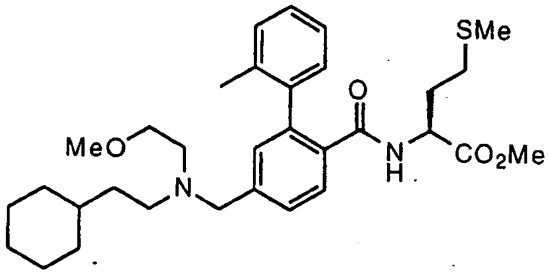


Example 1104B

N-(2-methoxyethyl)-N-2-cyclohexylethylamine

Using the procedure of example 1178F, example 1104A (1.70 g, 8.54 mmol) provided the title compound (1.56 g, 100%).

MS (DCI, NH_3): 186 (MH^+).



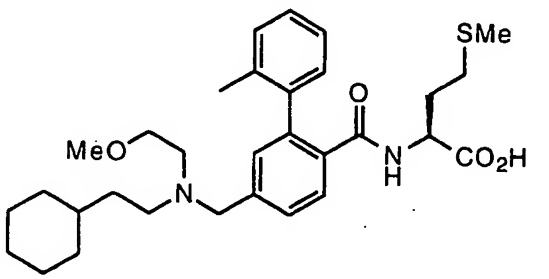
Example 1104C

N-[4-(N-(2-cyclohexylethyl)-N-2-methoxyethylaminomethyl)-2-(2-methylphenyl)benzoyl]methionine, methyl ester

Using the procedure of example 1103C, example 1104B (186 mg, 1.0 mmol) and example 403G (192 mg, 0.5 mmol) were combined to provide 78 mg (28%) of the title compound.

^1H NMR (300 MHz., $CDCl_3$): δ 7.91, dd, 1H; 7.42, dd, 1H; 7.18 - 7.37, m, 4H; 7.17, bs, 1H; 5.89, bd, 1H; 4.64, m, 1H; 3.68, s, 2H; 3.66, s, 3H; 3.45, t, 2H; 3.31, s, 3H; 2.66, t, 2H; 2.50, t, 2H; 2.19, s, 1.5H (o-tolyl); 2.07, s, 1.5H (o-tolyl); 2.05, m, 1H; 2.03, s, 1.5H (SMe); 2.01, s, 1.5H (SMe); 1.85, m, 1H; 1.63, bm, 6H; 1.34, m, 2H; 1.06 - 1.29, m, 4H; 0.88, m, 2H.

MS (ESI+): 555 (MH+): (ESI-): 553 (M-H).

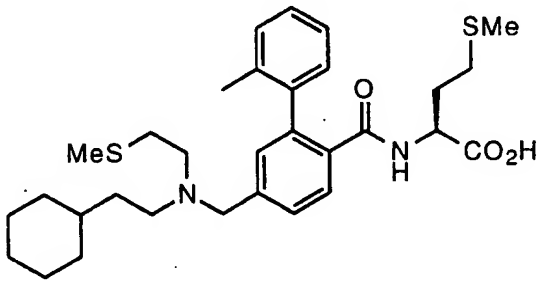


Example 1104D

N-[4-(N-(2-cyclohexylethyl)-N-2-methoxyethylaminomethyl)-2-(2-methylphenyl)benzoyl]methionine

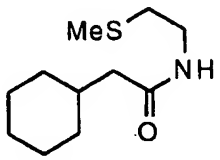
A solution of example 1104C (73 mg, 0.13 mmol) in 2 mL of 3:1 THF/methanol was cooled in an ice bath and treated with lithium hydroxide (0.26 mL of a 1M aqueous solution, 0.26 mmol) and the mixture stirred overnight and then concentrated. The solid was diluted with water and the pH adjusted to 4.5 with 1M aqueous phosphoric acid and then extracted with 3 portions of ethyl acetate. The combined organic fractions were washed with brine, dried filtered and concetrated. The residue was lyophilized to provide 70 mg of the title compound.

^{1}H NMR (300 MHz., CD_3OD): δ 7.74, d, 1H; 7.58, d, 1H; 7.37, m, 1H; 7.10 - 7.31, m, 4H; 4.50, m, 3H; 3.66, t, 2H; 3.37, s, 3H; 3.22, t, 2H; 3.04, m, 2H; 2.22, bs, 1H; 2.10, m, 3H; 1.97, s, 3H; 1.90, m, 2H; 1.53 - 1.77, m, 8H; 1.14 - 1.38, m, 4H; 0.96, m, 2H.
MS (ESI+): 541 (MH+): (ESI-): 539 (M-H). Calc'd for $C_{31}H_{44}N_2O_4S$•0.85 H_2O; C 66.96; H 8.28; N 5.04; Found: C 66.97; H 8.34; N 4.87.



Example 1105

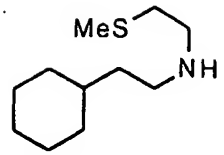
N-[4-(N-(2-cyclohexylethyl)-N-2-methylthioethylaminomethyl)-2-(2-methylphenyl)benzoyl]methionine



Example 1105A

N-(2-methylthioethyl)-2-cyclohexylacetamide

Following the procedure of example 1104A, 2-methylthioethylamine (1.0 g, 11 mmol) was converted to the title compound (1.77 g, 89%).
MS (DCI, NH_3): 216 (MH^+); 233 $(M+NH_4)^+$.

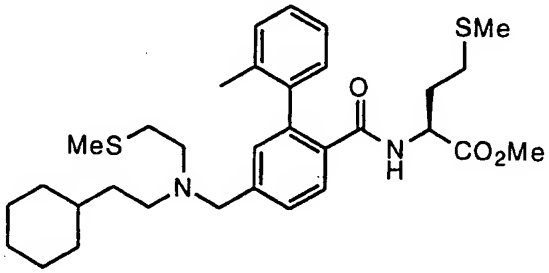


Example 1105B

N-(2-methylthioethyl)-2-cyclohexylethylamine

Using the procedure of example 1178F, example 1105A (1.75 g, 8.44 mmol) was converted into the title compound (1.63 g, 100%).

MS (DCI, NH_3): 202 (MH^+).



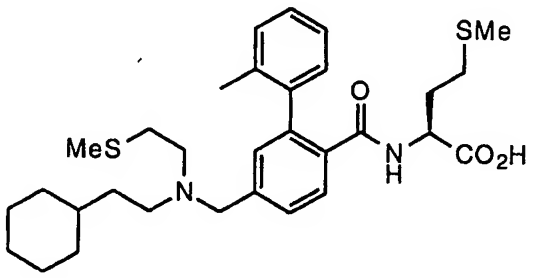
Example 1105C

N-[4-(N-(2-cyclohexylethyl)-N-2-methylthioethylaminomethyl)-2-(2-methylphenyl)benzoyl]methionine, methyl ester

Using the procedure of example 1103C, example 1105B (201 mg, 1.0 mmol) and example 403G (192 mg, 0.5 mmol) were combined to provide 151 mg (53%) of the title compound.

^1H NMR (300 MHz., $CDCl_3$): δ 7.91, dd, 1H; 7.42, dd, 1H; 7.18 - 7.37, m, 4H; 7.17, bs, 1H; 5.89, bd, 1H; 4.63, m, 1H; 3.66, s, 3H; 3.63, s, 2H; 2.68, m, 2H; 2.59, m, 2H; 2.48, t, 2H; 1.99 - 2.21, m, 10H; 1.85, m, 1H; 1.62, bm, 6H; 1.36, m, 2H; 1.06 - 1.30, m, 4H; 0.87, m, 2H.

MS (ESI+): 571 (MH+): (ESI-): 569 (M-H).



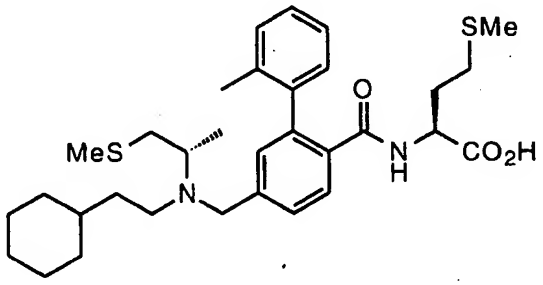
Example 1105D

N-[4-(N-(2-cyclohexylethyl)-N-2-methylthioethylaminomethyl)-2-(2-methylphenyl)benzoyl]methionine

A solution of example 1105C (145 mg, 0.25 mmol) in 2 mL of 3:1 THF/methanol was cooled in an ice bath and treated with lithium hydroxide (0.5 mL of a 1M aqueous solution, 0.5 mmol) and the mixture stirred overnight. The solution was concentrated to dryness and diluted with water and the pH adjusted to 4.5 with 1M aqueous phosphoric acid. The solid collected was by filtration and dried in the air to provide 130 mg (93%) of the title compound.

^{1}H NMR (300 MHz., CD_3OD): δ 7.71, d, 1H; 7.57, d, 1H; 7.35, d, 1H; 7.10 - 7.31, m, 4H; 4.32, m, 1H; 4.17, s, 2H; 3.10, m, 2H; 2.94, m, 2H; 2.76, m, 2H; 2.22, bs, 1H; 2.02 - 2.09, m, 3H; 2.10, s, 3H; 1.99, s, 3H; 1.89, m, 2H; 1.68, m, 6H; 1.56, m, 2H; 1.09 - 1.26, m, 4H; 0.93, m, 2H.

MS (ESI+): 557 (MH+): (ESI-): 555 (M-H). Calc'd for $C_{31}H_{44}N_2O_3S_2 \cdot 0.50\ H_2O$; C 65.80; H 8.02; N 4.95; Found: C 65.79; H 7.89; N 4.79.



Example 1106

N-[4-(N-(2-cyclohexylethyl)-N-1-methyl-2(S)-methylthioethylaminomethyl)-2-(2-methylphenyl)benzoyl]methionine

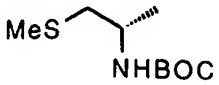
Example 1106A

2(S)-N-t-butoxycarbonylaminopropan-1-ol

A stirred solution of 2(S)-amino-1-propanol (1.0 g, 13.3 mmol) in 20 mL of methylene chloride was treated with di-tertbutyldicarbonate (3.19 g, 14.6 mmol) in 5 mL of methylene chloride and then the solution was treated with 10 mL of 2M aqueous sodium carbonate and stirred for 2 hours. The biphasic mixture was diluted with water and the layers were separated. The aqueous layer was extracted with methylene chloride and the combined organic layers were dried, filtered and concentrated to provide 2.35 g (105%) of the title compound.

^{1}H NMR (300 MHz., $CDCl_3$): δ 4.59, bs, 1H; 3.77, m, 1H; 3.64, dd, 1H; 3.52, dd, 1H; 2.42, bs, 1H; 1.44, s, 9H; 1.14, d, 3H.

MS (DCI, NH_3): 176 $(MH)^+$; 193 $(M+NH_4)^+$.



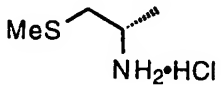
Example 1106B

1-Methylthio-2(S)-N-t-butoxycarbonylaminopropane

A stirred solution of example 1106A (350 mg, 2.0 mmol) in 6 mL of methylene chloride was cooled in an ice/acetone bath and sequentially treated with triethylamine (0.34 mL, 2.4 mmol) and methanesulfonyl chloride (0.17 mL, 2.2 mmol) and the mixture stirred for 2 hours and then diluted with ether, extracted with water, 1M aqueousphosphoric acid, brine, dried filterd and concentrated to provide a yellow oil that was used directly. The mesylate was dissolved in 2 mL of DMF and added to a mixture of sodium thiomethoxide (280 mg, 4.0 mmol) and 5 mL of DMF and the mixture was stirred for 2 hours. The reaction was quenched by the addition of water and the mixture diluted with water and ethyl acetate. The layers were separated and the mixture was extracted with 2 additional portions of ethyl acetate and the combined organic layers washed with water and brine, dried, filtered and concentrated to provide 328 mg (80% overall) of the title compound.

^{1}H NMR (300 MHz., $CDCl_3$): δ 3.86, bs, 1H; 2.65, dd, 1H; 2.56, dd, 1H; 2.14, s, 3H; 1.45, s, 9H; 1.22, d, 3H.

MS (DCI, NH_3): 206 $(MH)^+$; 223 $(M+NH_4)^+$.



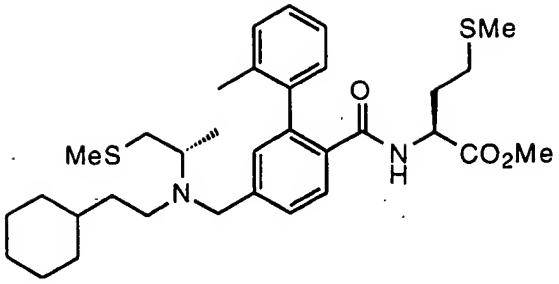
Example 1106C

1-Methylthio-2(S)-aminopropane hydrochloride salt

Example 1106B (320 mg, 1.56 mmol) was dissolved in 2 mL of 4N HCl/dioxane and stirred for 1 Hour. The mixture was diluted with ether and filtered to provide 103 mg (53%) of the title compound as a white solid.

^{1}H NMR (300 MHz., $CDCl_3$): δ 8.56, bs, 3H; 3.51, m, 1H; 2.89, dd, 1H; 2.78, dd, 1H; 2.17, s, 3H; 1.54, d, 3H.

MS (DCI, NH_3): 123 $(M+NH_4)^+$.



12235

Example 1106D

N-[4-(N-(2-cyclohexylethyl)-N-1-methyl-2(S)-methylthioethylaminomethyl)-2-(2-methylphenyl)benzoyl]methionine, methyl ester

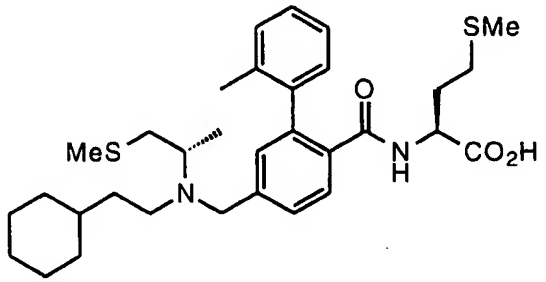
Part 1. Following the general procedure of example 403H, example 1106C (98 mg,
12240 0.69 mmol), example 403G (243 mg, 0.63 mmol), diisopropylethylamine (0.12 mL, 0.69 mmol) and acetic acid (0.18 mL, 3.14 mmol) were stirred in 4 mL of 1,2-dichloroethane for 2 hours and then treated with sodium triacetoxyborohydride (263 mg, 1.26 mmol). This procedure yielded 332 mg of material that was used in the next step.

Part 2. The amine prepared in part 1 was treated with 2-cyclohexylacetaldehyde (159
12245 mg, 1.26 mmol), acetic acid (0.36 mL, 6.3 mmol) and sitrred for 2 hours. This solution was treated with sodium triacetoxyborohydride (263 mg, 1.26 mmol) and the mixture stirred overnight. The mixture was quenched and worked-up as described in example 403H. The residue obtained was purified by cloumn chromatography on silica gel (20 g, 20% ethyl acetate/hexanes) to provide 225 mg (61% overall) of the title compound.

12250 ^{1}H NMR (300 MHz., $CDCl_3$): δ 7.89, dd, 1H; 7.47, d, 1H; 7.15 - 7.37, m, 5H; 5.87, bd, 1H; 4.63, m, 1H; 3.67, d, 1H; 3.65, s, 3H; 3.55, d, 1H; 2.96, m, 1H; 2.75, dd, 1H; 2.44, m, 2H; 2.37, dd, 1H; 1.99 - 2.22, m, 10H; 1.84, m, 1H; 1.60, m, 6H; 1.09 - 1.33, m, 6H; 1.08, d, 3H; 0.72 - 1.00, m, 2H.

MS (ESI+): 585 (MH+): (ESI-): 583 (M-H).

12255



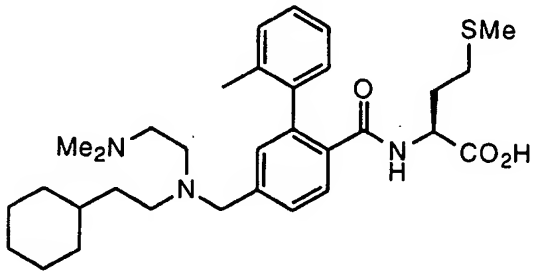
Example 1106

N-[4-(N-(2-cyclohexylethyl)-N-1-methyl-2(S)-methylthioethylaminomethyl)-2-(2-methylphenyl)benzoyl]methionine

Following the procedure of example 1105D, example 1106D (210 mg, 0.36 mmol) provided 110 mg (53%) of the title compound.

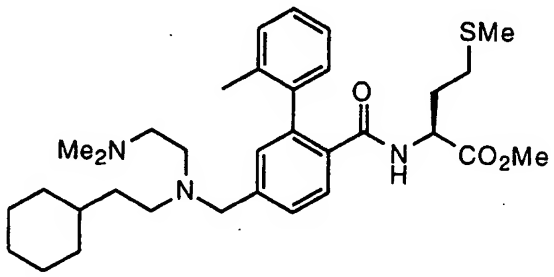
^{1}H NMR (300 MHz., CD_3OD): δ7.69, d, 1H; 7.56, bd, 1H; 7.37, bd, 1H; 7.09 - 7.32, m, 4H; 4.33, m, 1H; 4.16, m, 1H; 4.00, m, 1H; 3.32, dt, 1H; 2.89, m, 3H; 2.64, m, 1H; 2.23, bs, 1H; 2.06, m, 2H; 2.04, s, 3H; 1.98, s, 3H; 1.89, m, 2H; 1.65, m, 6H; 1.44, m, 2H; 1.32, d, 3H; 1.28, m, 3H; 0.88, m, 2H.

MS (ESI+): 571 (MH+): (ESI-): 569 (M-H). Calc'd for $C_{32}H_{46}N_2O_3S_2$; C 67.33; H 8.12; N 4.91; Found: C 67.12; H 8.10; N 4.70.



Example 1107

N-[4-(N-(2-cyclohexylethyl)-N-2-N,N-dimethylaminomethyl)-2-(2-methylphenyl)benzoyl]methionine



Example 1107A

N-[4-(N-(2-cyclohexylethyl)-N-2-N,N-dimethylaminomethyl)-2-(2-methylphenyl)benzoyl]methionine, methyl ester

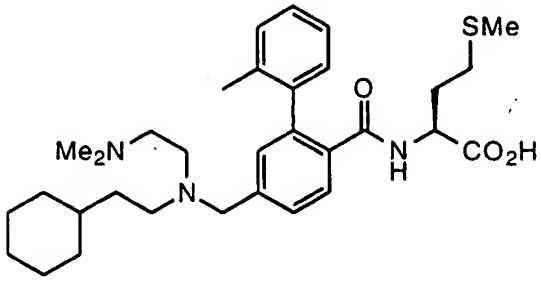
Part 1. Following the procedure of example 1106D, part 1, example 403G (550 mg, 1.43 mmol) and 2-N,N-dimethylaminoethylamine (0.31 mL, 2.86 mmol) and acetic acid (0.82 mL, 14.3 mmol) gave the coressponding secondary amine (673 mg).

Part 2. Following the procedure of example 1106D part 2, the amine produced in example 1107A, part 1 (660 mg, 1.44 mmol) and 2-cyclohexyacetaldehyde (364 mg, 2.88 mmol) gave a material that was purified by column chromatography on silica gel (25 g, ethyl

acetate then 90/10/0.1 ethyl acetate/methanol/conc. aq. ammonia) providing 498 mg (60% overall) of the title compound.

^{1}H NMR (300 MHz., $CDCl_3$): δ 790, dd, 1H; 7.41, dd, 1H; 7.18 - 7.34, m, 4H; 7.16, bs, 1H; 5.88, bs, 1H; 4.62, m, 1H; 3.65, s, 3H; 3.63, s, 2H; 2.57, m, 2H; 2.47, m, 2H; 2.39, m, 2H; 2.21, s, 6H; 1.99, 2.28, m, 7H; 1.86, m, 1H; 1.63, bm, 6H; 1.35, m, 2H; 1.20 m, 2H; 1.14, m, 2H; 0.85, m, 2H.

MS (ESI+): 568 (MH+): (ESI-): 566 (M-H).



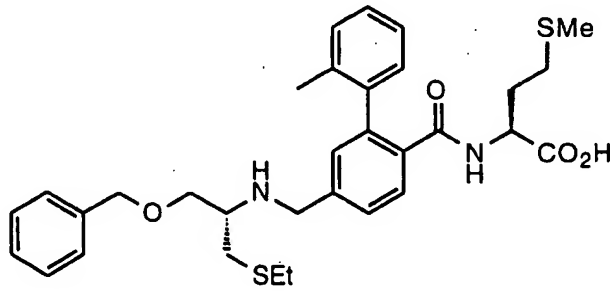
Example 1107B

N-[4-(N-(2-cyclohexylethyl)-N-2-N,N-dimethylaminomethyl)-2-(2-methylphenyl)benzoyl]methionine

Following the procedure of example 1104D, example 1107A (485 mg, 0.85 mmol) provided 382 mg (81%) of the title compound as a white lyophilate.

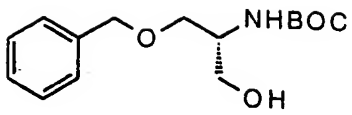
^{1}H NMR (300 MHz., CD_3OD): δ 7.66, d, 1H; 7.46, d, 1H; 7.05 - 7.33, m, 5H; 4.35, m, 1H; 3.74, s, 2H; 3.17, t, 1H; 2.82, t, 2H; 2.75, s, 6H; 2.60, m, 2H; .24, bs, 1H; 1.94 - 2.12, m, 6H; 1.85, m, 2H; 1.67, m, 6H; 1.45, m, 2H; 1.21, m, 4H; 0.92, m, 2H.

MS (ESI+): 554 (MH+): (ESI-): 552 (M-H). Calc'd for $C_{32}H_{47}N_3O_3S \cdot 1.00\ H_2O$; C 67.22; H 8.64; N 7.35; Found: C 67.23; H 8.43; N 7.26.



Example 1108

N-[4-(N-(1-benzyloxymethyl-2(S)-ethylthioethylaminomethyl)-2-(2-methylphenyl)benzoyl]methionine

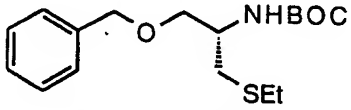


Example 1108A

1-benzyloxy-2(S)-t-butoxycarbonylamino-3-hydroxypropane

N-BOC-O-benzylserine (5.0 g, 16.9 mmol) in 30 mL dimethoxyethane was treated with 4-methylmorpholine (2.0 mL, 18.6 mmol) and cooled to 0°C. The solution was treated with isobutylchloroformate (2.3 mL, 17.8 mmol) and the resulting suspension stirred for 15 minutes, then filtered. The solids collected were washed with 2 portions of dimethoxyethane and the washings combined with the original filtrate. This material was cooled in an ice bath and treated with a cold solution of sodium borohydride (1.93 g, 50.8 mmol) in 40 mL 1/2 saturated sodium bicarbonate and the reaction stirred for 2 hours. The mixture was diluted with water and extracted with 3 portions of ethyl acetate. The combined organic extracts were washed with saturated aqueous sodium bicarbonate, water and brine, dried, filtered and concentrated to provide the title compound.

MS (DCI, NH_3): 282 (MH^+); 299 $(M+NH_4)^+$.

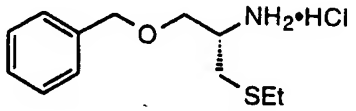


Example 1108B

1-benzyloxy-2(S)-t-butoxycarbonylamino-3-ethylthiopropane

Following the procedure described in example 1106B (and substituting potassium thioethoxide for sodium thiomethoxide), example 1108A (322 mg, 1.5 mmol) was converted to 342 mg (70% overall) the title compound.

MS (DCI, NH_3): 326 (MH^+); 343 $(M+NH_4)^+$.

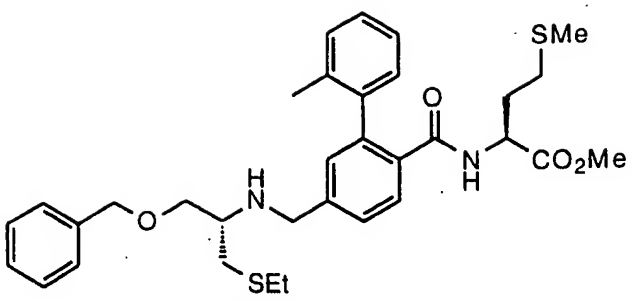


Example 1108B

1-benzyloxy-2(S)-amino-3-ethylthiopropane hydrochloride salt

Following the procedure described in example 1106C, example 1108B (342 mg, 1.05 mmol) was converted to 244 mg (89%) of the title compound.

MS (DCI, NH_3): 226 (MH^+).

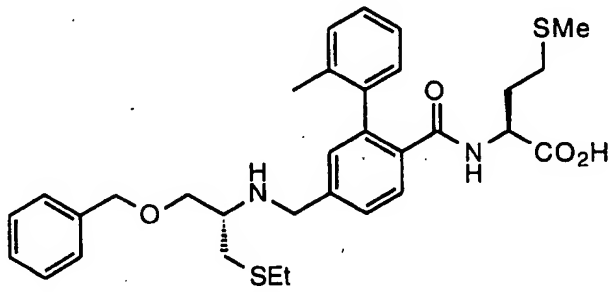


Example 1108C

N-[4-(N-(1-benzyloxymethyl-2(S)-ethylthioethylaminomethyl)-2-(2-methylphenyl)benzoyl]methionine, methyl ester

Following the procedure described in example 1106D, part 1, example 1108C (144 mg, 0.55 mmol), example 403G (192 mg, 0.50 mmol), diisopropylethylamine (0.098 mL, 0.55 mmol) and acetic acid (0.14 mL, 2.5 mmol) and sodium triacetoxyborohydride (213 mg, 1.0 mmol) provided 196 mg (66%) of the title compound after chromatography (silica gel, 20 g, 50% ethyl acetate/hexanes).

MS (ESI+): 595 (MH+): (ESI-): 593 (M-H).



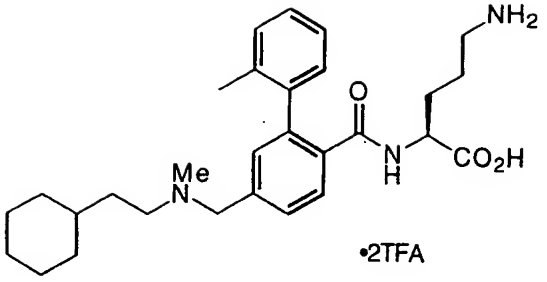
Example 1108D

N-[4-(N-(1-benzyloxymethyl-2(S)-ethylthioethylaminomethyl)-2-(2-methylphenyl)benzoyl]methionine

Following the procedure of example 1104D, example 1108C (187 mg, 0.31 mmol) provided 175 mg of the title compound.

^{1}H NMR (300 MHz., CD_3OD): δ 7.70, d, 1H; 7.50, d, 1H; 7.08 - 7.39, m, 10H; 4.59, s, 2H; 4.29, m, 1H; 4.20, s, 2H; 3.70, d, 2H; 3.37, m, 1H; 2.85, d, 2H; 2.49, m, 2H; 2.21, bs, 1.5H; 2.08, s, 1.5H; 2.03, m, 1H; 1.98, s, 3H; 1.87, m, 2H; 1.68, m, 1H; 1.20, t, 3H.

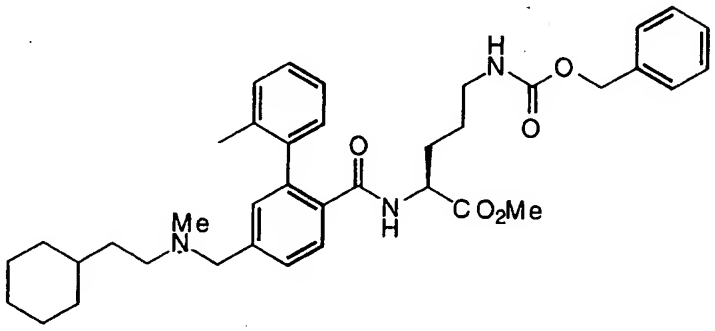
MS (ESI+): 581 (MH+): (ESI-): 579 (M-H). Calc'd for $C_{32}H_{40}N_3O_4S_2$; C 66.18; H 6.94; N 4.82; Found: C 65.52; H 6.76; N 4.58.



Example 1110

N-[4-(N-(2-Cyclohexylethyl)-N-methylaminomethyl)-2-(2-methylphenyl)benzoyl]ornithine, Trifluoroacetate salt

12370



Example 1110A

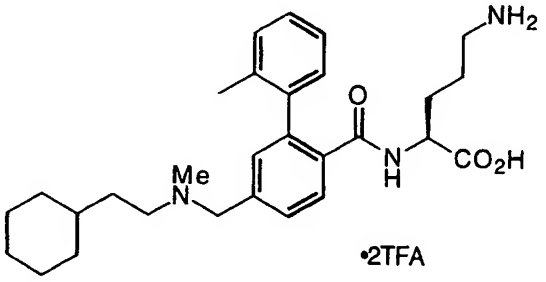
N-[4-(N-(2-Cyclohexylethyl)-N-methylaminomethyl)-2-(2-methylphenyl)benzoyl]-N'-carbobenzyloxyornithine, Methyl Ester

12375 The title compound was prepared according to the procedure in example 608D, replacing L-methionine methyl ester·HCl with L-N'-carbobenzyloxyornithine methyl ester•HCl, and was isolated as a colorless oil.

MS (ESI(+)) m/e 628 $(M+H)^+$.

MS (ESI(-)) m/e 626 $(M-H)^-$.

12380



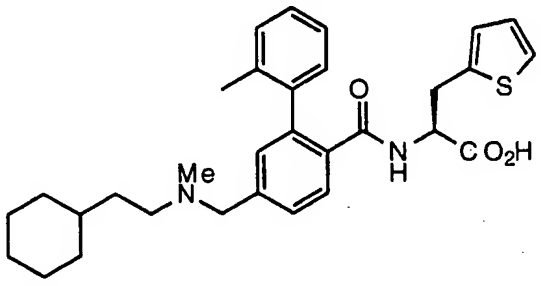
Example 1110B

N-[4-(N-(2-Cyclohexylethyl)-N-methylaminomethyl)-2-(2-methylphenyl)benzoyl]ornithine, Trifluoroacetate salt

To a solution of N-[4-(N-(2-cyclohexylethyl)-N-methylaminomethyl)-2-(2-methylphenyl)benzoyl]-N'-carbobenzyloxyornithine methyl ester (270mg) in methanol (1.4mL) was added 5M LiOH (0.103mL). After 4h, the reaction was concentrated and the residue was dissolved in ethanol (3mL), followed by the addition of freshly distilled cyclohexene (0.1mL), then 10% palladium on carbon (50mg). The reaction vessel was tightly sealed and warmed to 80°C for 1h. Analytical HPCL analysis indicates ca. 30% conversion to the title compound. The reaction was filtered and concentrated, and the hydrogenation protocol was repeated twice. Analytical HPCL analysis of the resulting mixture still indicated low conversion. The reaction was filtered and concentrated, and the residue was dissolved in a minimum of 10%methanol/water, and purified by preparative reverse-phase medium pressure liquid chromatography, eluting with a gradient of methanol/water/0.1%TFA. Lyophylization of the appropriate fractions afforded the title compound as a light yellow powder (38mg).

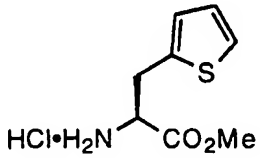
^{1}H NMR (300 MHz, DMSO) δ 0.83-0.97 (m, 2H), 1.08-1.83 (m, 15H), 2.07-2.14 (m, 4H), 2.62-2.73 (m, 4H), 2.95-3.24 (m, 2H), 4.09-4.17 (m, 1H), 4.22-4.49 (m, 2H), 7.09-7.27 (m, 4H), 7.40 (s, 1H), 7.54-7.73 (m, 5H), 8.40 (brd, J=5 Hz, 1H), 9.68 (brs, 1H).

MS (APCI(-)) m/e 478 (M-H).



Example 1112

N-[4-(N-(2-cyclohexylethyl)-N-2-N-methylaminomethyl)-2-(2-methylphenyl)benzoyl]thien-2-ylalanine

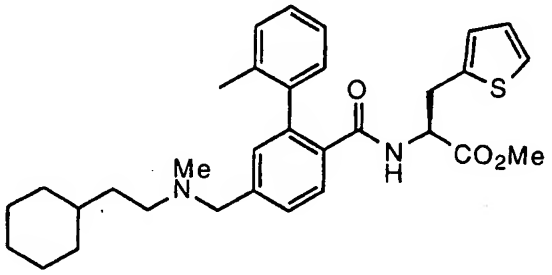


Example 1112A

3-(2-thienyl)-L-alanine, methylester hydrochloride

A solution of 3-(2-thienyl)-L-alanine (200 mg, 1.17 mmol) in 3 mL of methanol was treated with chlorotrimethylsilane (0.73 mL, 5.84 mmol) and the mixture heated to reflux for 60 hours. The solution was then concentrated to provide 257 mg (99%) of the title compound.

MS (DCI, NH_3): 186 (MH^+); 203 $(M+NH_4)^+$.

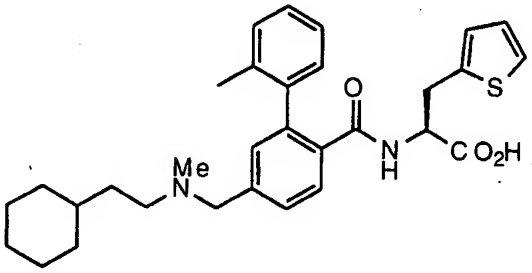


Example 1112B

N-[4-(N-(2-cyclohexylethyl)-N-2-N-methylaminomethyl)-2-(2-methylphenyl)benzoyl]thien-2-ylalanine

Following the procedure of example 608D, example 1112A (122 mg, 0.55 mmol) and example 608C (183 mg, 0.5 mmol) were converted to 154 mg (58%) of the title compound.

MS (ESI+): 533 (MH+): (ESI-): 531 (M-H).



Example 1112C

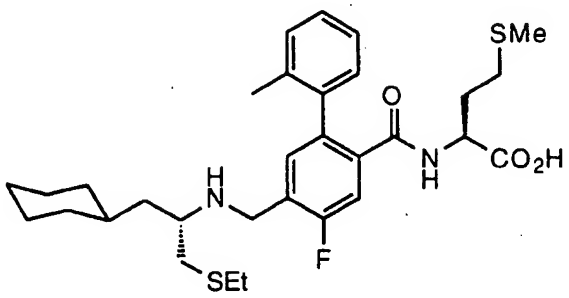
N-[4-(N-(2-cyclohexylethyl)-N-2-N-methylaminomethyl)-2-(2-methylphenyl)benzoyl]thien-2-ylalanine

Following the procedure of example 1105D, example 1112C (150 mg, 0.28 mmol) provided 124 mg (85%) of the title compound.

^1H NMR (300 MHz., CD_3OD): δ 7.69, m, 1H; 7.52, dd, 1H; 7.31, bs, 1H; 7.21, m, 2H; 7.14, m, 3H; 6.85, bt, 1H; 6.72, m, 1H; 4.40, m, 1H; 4.24, bd, 2H; 3.10 - 3.27, m, 2H; 3.06, m, 2H; 2,72, s, 3H; 2.08, s, 3H; 1.56 - 1.76, m, 7H; 1.13 - 1.37, m, 4H; 0.96, m, 2H.

MS (ESI+): 519 (MH+): (ESI-): 517 (M-H). Calc'd for $C_{31}H_{38}N_2O_3S \cdot 0.75\ H_2O$; C 69.96; H 7.48; N 5.26; Found: C 70.01; H 7.38; N 5.19.

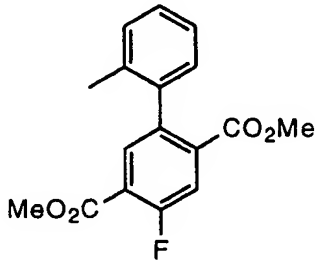
12440



Example 1134

N-[4-(1-ethylthio-3-cyclohexylprop-2-ylaminomethyl)-5-fluoro-2-(2-

12445 methylphenyl)benzoyl]methionine



Example 1134A

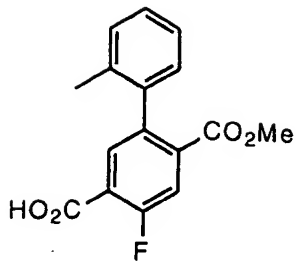
Dimethyl 2-(2-Methylphenyl)-5-fluoroterephthalate

12450 A stirred solution of the product from example 319B (2.99 g, 10.00 mmol) in in 30 ml of dioxane was cooled in an ice bath and 6.5 ml of a 48% aqueous solution of tetrafluoroboric acid was added. The resulting solution was treated with t-butylnitrite such that the internal temperature did not exceed 10°C and stirring was continued for 30 minutes further. The mixture was carefully diluted with ether (~200 mL) and the solid collected by

12455 filtration. The dried solid was suspended in 20 mL of isooctane and heated to reflux overnight and then diluted with 5 mL of dioxane and heating continued for 1 hour more. The resulting dark mixture was cooled to ambient temperature and concentrated. The residue was purified by column chromatography on silica gel (50g, 5% ethyl acetate/hexanes) to provide 0.87 g (29%) of the title compound.

12460 ^{1}H NMR (300 MHz., $CDCl_3$): δ 7.73, d, 1H; 7.72, d, 1H; 7.15 - 7.32, m, 3H; 7.06, d, 1H; 3.94, s, 3H; 3.65, s, 3H; 2.07, s, 3H.

MS (DCI-NH_3): 320 ($M+NH_4H^+$).



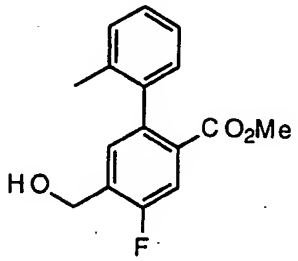
Example 1134B

2-(2-Methylphenyl)-4-carboxy-5-fluorobenzoic acid, methyl ester

A solution of example 1134A (0.87 g, 2.88 mmol) in 10 mL of 4:1 THF/methanol was treated with 3 mL of 1M aqueous lithium hydroxide and the mixture stirred at ambient temperature for 60 hours. The solution was made acidic by the addition of excess 3N aqueous HCl and then extracted with 3 portions of ethyl acetate. The combined organic extracts were washed with water and brine, dried, filtered and concentrated to provide 0.77 g (92%) ofthe title compound sufficiently pure to use in the next step.

^{1}H NMR (300 MHz., CD_3OD): δ 7.7.74, d, 1H; 7.69, d, 1H; 7.15 - 7.28, m, 3H; 7.03, q, 1H; 3.61, s, 3H; 2.07, s, 3H.

MS (DCI, NH_3): 306 (M+ NH_4^+).

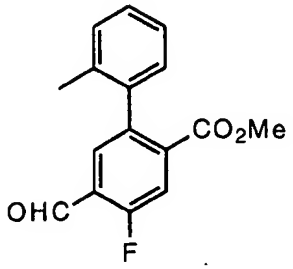


Example 1134C

2-(2-Methylphenyl)-4-hydroxymethyl-5-fluorobenzoic acid, methyl ester

A solution of example 1134B (760 mg, 2.64 mol) in 5 mL of dimethoxyethane was treated with 4-methylmorpholine (0.32 mL, 2.90 mmol) and the mixture cooled in an ice bath. The clear solution was then treated with isobutylchloroformate (0.36 mL, 2.77 mmol) and the suspension stirred for 30 minutes. The mixture was filtered and the solids washed with 2 portions of THF and the combined filtrates recooled in an ice bath. The cold solution was treated with a mixture of sodium borohydride (300 mg, 7.92 mmol) in 3 mL of 1/2 saturated sodium bicarbonate and the mixture stirred for 2 hours. The mixture was diluted with water and extracted with 3 portions of ethyl acetate. The combined organic extracts were washed with water and brine, dried, filtered and concentrated. The residue was purified by column chromatography of silica gel (35 g, 25% ethyl acetate/hexanes) to provide 527 mg (73%) of the title compound.

^{1}H NMR (300 MHz., $CDCl_3$): δ 7.67, d, 1H; 7.44, d, 1H; 7.15 - 7.28, m, 3H; 7.05, d, 1H; 4.83, d, 1H; 3.62, s, 3H; 2.07, s, 3H; 1.94, bt, 1H.
MS (DCI, NH_3): 292 (M+ NH_4^+).

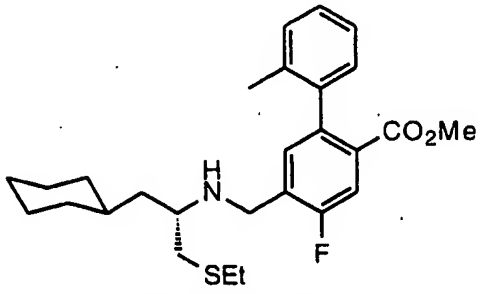


Example 1134D

2-(2-Methylphenyl)-4-formyl-5-fluorobenzoic acid, methyl ester

A stirred solution of example 1134C (515 mg, 1.79 mmol) in 2 mL of methylene chloride was treated with KBr (21 mg, 0.18 mmol), 2 mL of water and sodium bicarbonate (0.5 g) and then cooled in an ice bath. The mixture was treated with TEMPO (3 mg, 0.02 mmol) and then commercial bleach (Chlorox, 3.1 mL) was added such that the temperature did not exceed 5°C. The mixture was stirred for 10 minutes at which time an additional 1.5 mL of Chlorox was added. After stirring a further 10 minutes, the mixture was diluted with water and layers were separated. The aqueous phase was extracted with 1 portion of methylene chloride and the combined organic phases were extracted with 5% aqueous sodium bisulfite, dried, filtered and concentrated to give 478 mg (93%) of the title compound.

^{1}H NMR (300 MHz., $CDCl_3$): δ 10.43, s, 1H; 7.77, d, 1H; 7.73, d, 1H; 7.17 - 7.31, m, 3H; 7.05, m, 1H; 3.63, s, 3H; 2.06, s, 3H.
MS (DCI, NH_3): 290 (M+ NH_4^+).



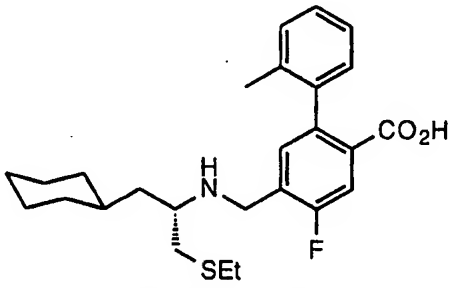
Example 1134E

N-[4-(1-ethylthio-3-cyclohexylprop-2-ylaminomethyl)-5-fluoro-2-(2-methylphenyl)benzoic acid methyl ester

Example 1134D (143 mg, 0.5 mmol) was dissolved in 2 mL of 1,2-dichloroethane and the amine hydrochloride salt from example 403D (178 mg, 0.75 mmol), diisopropylethylamine (0.13 mL, 0.75mmol) and acetic acid (0.15 mL, 2.50 mmol) were sequentially added. The mixture was stirred at ambient temperature for 4 hours and then treated with sodium triacetoxyborohydride (213 mg, 1.0 mmol) and the mixture stirred overnight. The reaction was quenched by the addition of 2 mL of 2M aqueous sodium carbonate and the mixture stirred vigorously for 1hour and then diluted with water and methylene chloride. The aqueous layer was extracted with methylene chloride and the combined organic layers dried, filtered and concentrated. The residue was purified by column chromatography on silica gel (20g, 15% ethyl acetate/hexanes) to provide 165 mg (72%) of the title compound.

^{1}H NMR (300 MHz., $CDCl_3$): δ 7.67, d, 1H; 7.16 - 7.31, m, 5H; 7.04, bd, 1H; 3.93, s, 2H; 3.63, s, 3H; 2.76, m, 2H; 2.57, m, 1H; 2.46, q, 2H; 2.06, s, 3H; 1.63, bm, 6H; 1.37, bm, 3H; 1.22, t, 3H; 1.13, m, 2H; 0.87, m, 2H.

MS (ESI +): 458 (MH^+); (ESI-) 456 (M-H).

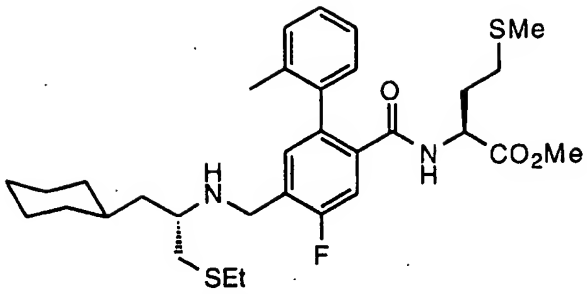


Example 1134F

N-[4-(1-ethylthio-3-cyclohexylprop-2-ylaminomethyl)-5-fluoro-2-(2-methylphenyl)benzoic acid

Example 1134E (160 mg, 0.35 mmol) was dissolved in 1.5 mL of ethanol and aqueous sodium hydroxide was added (1.75 mL of a 4N solution) and the mixture heated to reflux for 3 hours. The cooled solution was concentrated to dryness and dissoved in water and the pH adjusted to ~ 4 with 1M aqueous phosphoric acid. The mixture was extracted with 3 portions of ethyl acetate and the combined organic extracts were washed with brine, dried, filtered and concentrated to provide 164 mg (105%) of the title compound.

^{1}H NMR (300 MHz., CD_3OD): δ 7.78, d, 1H; 7.43, d, 1H; 7.15 - 7.27, m, 3H; 7.06, bd, 1H; 4.42, m, 2H; 3.48, m, 1H; 3.00, dd, 1H; 2.93, dd, 1H; 2.58, q, 2H; 2.09, s, 3H; 1.63 -0 1.79, m, 7H; 1.45, bm, 2H; 1.14 - 1.36, m, 6H; 0.84 - 1.09, m, 2H.

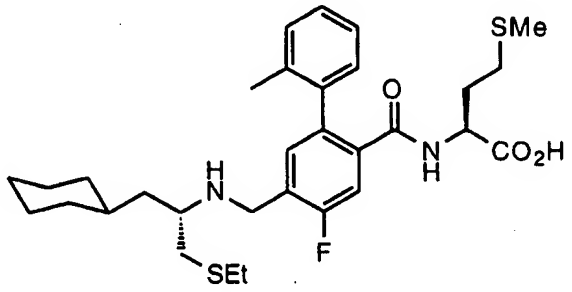


Example 1134G

N-[4-(1-ethylthio-3-cyclohexylprop-2-ylaminomethyl)-5-fluoro-2-(2-methylphenyl)benzoyl]methionine, methyl ester

According to the procedure described in example 1178I, example 1134F (160 mg, 0.35 mmol) provided 140 mg (68%) of the title compound after column chromatographic purification on silica gel (20 g, 35% ethyl acetate/hexanes).

^{1}H NMR (300 MHz., $CDCl_3$): δ 7.70, dd, 1H; 7.14 - 7.38, m, 5H; 5.91, bd, 1H; 4.60, m, 1H; 3.94, s, 2H; 3.66, s, 3H; 2.77, m, 2H; 2.58, m, 1H; 2.46, q, 2H; 2.28, s, 1.5 H(o-tolyl rotamer); 2.07, s, 1.5H (o-tolyl rotamer); 1.95 - 2.10, m, 5H; 1.84, m, 2H; 1.50 - 1.72, m, 6H; 1.26 - 1.48, m, 3H; 1.21, t, 3H; 1.04 - 1.26, m, 3H; 0.88, m, 2H. MS: (ESI-): 587 (M-H).



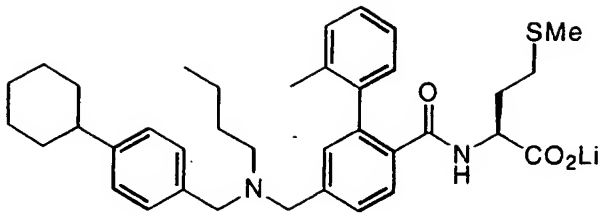
Example 1134H

N-[4-(1-ethylthio-3-cyclohexylprop-2-ylaminomethyl)-5-fluoro-2-(2-methylphenyl)benzoyl]methionine

Following the procedure of example 1105D, example 1134G (130 mg, 0.22 mmol) provided 94 mg (75%) of the title compound.

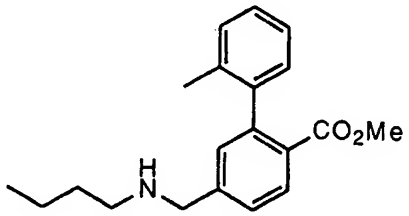
^{1}H NMR (300 MHz., CD_3OD): δ 7.52, d, 1H; 7.39, m, 1H; 7.10 - 7.30, m, 4H; 4.29, m, 1H; 4.25, q, 2H; 3.24, m, 1H; 2.89, dd, 1H; 2.78, dd, 1H; 2.52, q, 2H; 2.22, bs, 1.5H; 2.08, bs, 1.5H; 2.05, m, 1H; 1.98, s, 3H; 1.89, m, 2H; 1.69, m, 6H; 1.58, t, 2H; 1.43, m, 1H; 1.25, m, 1H; 1.22, t, 3H; 0.90, m, 2H.

MS (ESI+): 575 (MH+): (ESI-): 573 (M-H). Calc'd for $C_{31}H_{43}FN_2O_3S_2 \cdot 0.35\ H_2O$; C 64.07; H 7.58; N 4.82; Found: C 64.08; H 7.54; N 4.65.



Example 1136

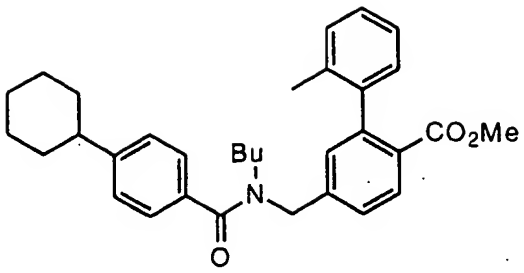
N-[4-(N-butyl-N-4-cyclohexylbenzylaminomethyl)-2-(2-methylphenyl)benzoyl]methionine lithium salt



Example 1136A

Methyl 4-(N-Buytylaminomethyl)-2-(2-methylphenyl)benzoate

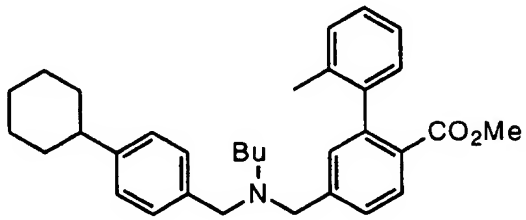
To a 0 °C solution of intermediate 1178B (1.0 g, 3.71 mmol) in DCM (10 mL) was added oxallyl chloride (2.0 M in DCM, 3.7 mL), and a drop of DMF. The reaction was stirred at room temperature for 2 hours, and was then evaporated to dryness. The residue was redesolved in DCM (10 mL), and was cooled to 0 °C. To it was slowly added butylamine (0.5 mL). The reaction mixture was stirred for 5 min., and then was filtered through silca gel (10 g), rinsed with ethyl acetate, and concentrted. The solid was desolved in THF (10 ML), and to it was added borane (1.0 M in THF, 5.0 mL), and the reaction mixture was reluxed for 15 hours. Methanol (0.5 mL) was added dropwisly to the reaction, followed by concentrated HCl (1 mL), and the mixture was heated at 60 °C for 1 hour. Then it was cooled to room temperature, the reaction mixture was adjusted to pH about 12-14 with sodium carbonate (2.0 M in water). The reaction mixture was then partitioned between ethyl acetate (50 mL) and water (5 mL). The organic layer was washed with water (10 mL), brine (20 mL), dried over anhydrous magnesium sulfate, filtered and concentrated to give the intermediate amine. The amine was used without further purification.



Example 1136B

Methyl 4-[N-butyl-N-(4-cyclohexylbenzylcarbonyl)aminomethyl]-2-(2-methylphenyl)benzoate

To a 0 °C solution of 4-cyclohexylbenzoic acid (204 mg, 1.0 mmol) in DCM (3 mL) was added oxallyl chloride (2.0 M in DCM, 1.0 mL), and a drop of DMF. The reaction was stirred at room temperature for 2 hours, and was then evaporated to dryness. The residue was redesolved in DCM (10 mL), and was cooled to 0 °C. To it was slowly added the intermediate 1136A (156 mg, 0.5 mmol) and triethylamine (202 mg, 2.0 mmol) in DCM (3 mL). The reaction mixture was stirred for 5 min., and then was filtered through silca gel (10 g), rinsed with ether, and concentrted. The residue was purified by column chromatography with 20% ethyl acetate in to give the title compound (165 mg, 66%). ^{1}HNMR (300 MHz, $CDCl_3$) δ 7.95 (d, 1 H), 7.32-7.16 (m, 9 H), 7.05 (br d, 1 H), 5.85-5.55 (loop, 2 H), 3.61 (s, 3 H), 3.47-3.17 (broad loop, 2 H), 2.49 (m, 1 H), 2.06 (s, 3 H), 1.90-0.70 (m, 17 H). MS(CI/NH_3) m/z: 498 $(M+H)^+$.

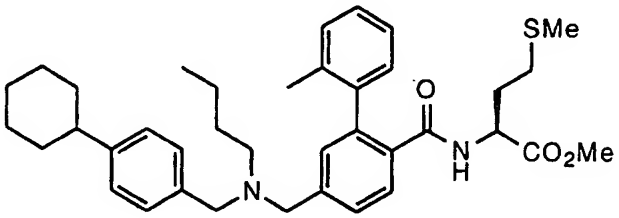


Example 1136C

Methyl 4-(N-Butyl-N-4-cyclohexylbenzylaminomethyl)-2-(2-methylphenyl)benzoate

To a solution of intermediate 1136B (93 mg) in THF (2 ML) was added borane (1.0 M in THF, 1.0 mL), and the reaction mixture was reluxed for 15 hours. Methanol (0.5 mL) was added dropwisly to the reaction, followed by concentrated HCl (0.5 mL), and the mixture was heated at 60 °C for 1 hour. Then it was cooled to room temperature, and was adjusted to pH about 12-14 with sodium carbonate (2.0 M in water). The reaction mixture was then partitioned between ethyl acetate (50 mL) and water (5 mL). The organic layer was washed with water (10 mL), brine (20 mL), dried over anhydrous magnesium sulfate, filtered and concentrated to give the title amine (88 mg, 94%). ^{1}HNMR (300 MHz, $CDCl_3$)

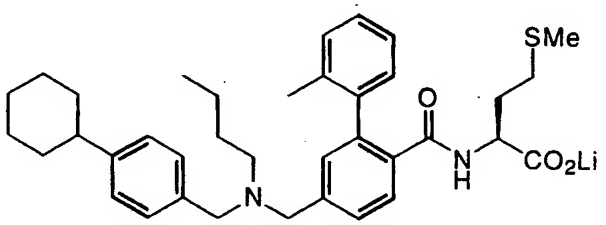
δ 7.90 (d, 1 H), 7.42 (dd, 1 H), 7.30-7.15 (m, 4 H), 7.12 (m, 2 H), 7.06 (m, 1 H), 3.59 (s, 2 H), 3.57 (br s, 2 H), 3.53 (br s, 2 H), 2.47 (m ,1 H), 2.41 (t, 2 H), 2.05 (s, 3 H), 1.90-1.20 (m, 14 H), 0.94 (t, 3 H). MS(CI/NH_3) m/z: 484 $(M+H)^+$.



Example 1136D

N-[4-(N-Butyl-N-4-cyclohexylbenzylaminomethyl)-2-(2-methylphenyl)benzoyl]methionine Methyl Ester

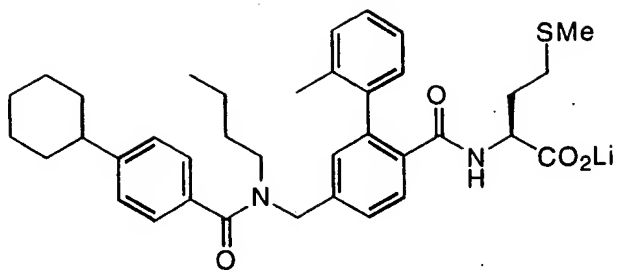
The procedures descriped in the Example 403E and 403F were used here to convert above intermediate 1136C (85 mg) to the title methyl ester 1136D (73 mg, 68%). ^{1}HNMR (300 MHz, $CDCl_3$) δ 7.90 (2 d's 1 H), 7.45 (br d, 1 H), 7.35-7.22 (m, 6 H), 7.19 (br s, 1 H), 7.13 (br d, 2 H), 5.85 (m, 1 H), 4.62 (m, 1 H), 3.65 (s, 3 H), 3.57 (s, 2 H), 3.53 (s, 2 H), 2.48 (m, 1 H), 2.41 (t, 2 H), 2.20-2.00 (4 s's, 6 H), 2.05 (m, 2 H), 1.92-1.20 (m, 16 H), 0.82 (t, 3 H). MS(CI/NH_3) m/z: 615 $(M+H)^+$.



Example 1136E

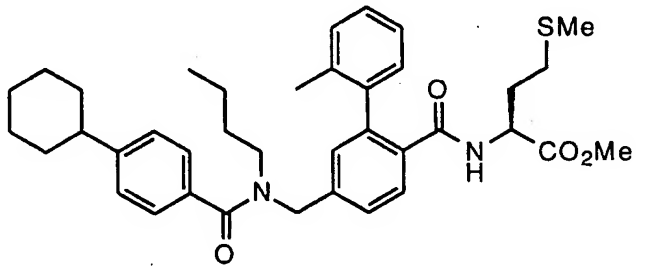
N-[4-(N-butyl-N-4-cyclohexylbenzylaminomethyl)-2-(2-methylphenyl)benzoyl]methionine lithium salt

The procedure descriped in the Example 403I was used here to convert the intermediate 1136D (64 mg) to the title lithium salt (64 mg, 100%). ^{1}H NMR (300 MHz, dmso-d_6) δ 7.49 (d, 1 H), 7.37 (br d, 1 H), 7.25-7.09 (m, 9 H), 6.91 (d, 1 H), 3.63 (m, 1 H), 3.56 (br s, 2 H), 3.47 (br s, 2 H), 2.45 (m, 1 H), 2.37 (t, 2 H), 2.17-1.98 (m, 8 H), 1.81-1.17 (m, 16 H), 0.76 (t, 3 H). MS(ESI–) m/z: 599 $(M-H)^-$.



Example 1137

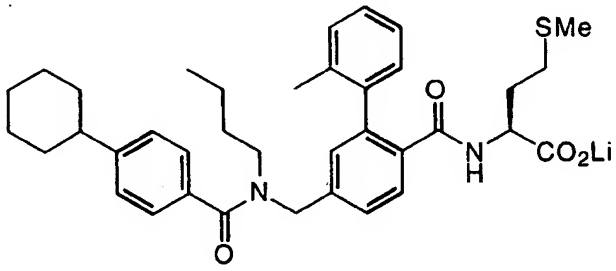
N-[4-(N-Butyl-N-4-cyclohexylbenzoylaminomethyl)-2-(2-methylphenyl)benzoyl]methionine lithium salt



Example 1137A

N-[4-(N-butyl-N-4-cyclohexylbenzoylaminomethyl)-2-(2-methylphenyl)benzoyl]methionine Methyl Ester

The procedures descriped in the Example 403E and 403F were used here to convert intermediate 1136B (63 mg) to the title methyl ester 1137A (72 mg, 90%). ^{1}HNMR (300 MHz, $CDCl_3$) δ 7.94 (2 d's 1 H), 7.37-7.15 (m, 10 H), 5.89 (m, 1 H), 4.80 (m, 1 H), 4.61 (br. loop, 2 H), 3.66 (s, 3 H), 3.43,3.22 (2 br loops, 2 H), 2.50 (m, 1 H), 2.20-2.00 (m, 8 H), 1.92-1.00 (m, 16 H), 0.96-0.70 (2 br loops, 3 H). MS(CI/NH_3) m/z: 629 $(M+H)^+$.



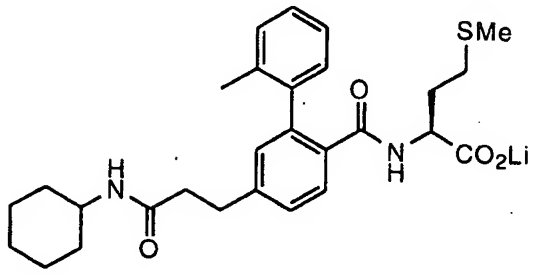
Example 1137B

N-[4-(N-Butyl-N-4-cyclohexylbenzoylaminomethyl)-2-(2-methylphenyl)benzoyl]methionine lithium salt

The procedure descriped in the Example 403I was used here to convert the intermediate 1137B (68 mg) to the title lithium salt (67 mg, 100%). ^{1}H NMR (300 MHz,

dmso-d_6) δ 7.53 (br d, 1 H), 7.42-7.08 (m, 9 H), 6.97 (m, 1 H), 6.95 (br d, 1 H), 4.72,4.57 (2 br. loops, 2 H), 3.65 (m, 1 H), 3..17 (br loop, 2 H), 2.50 (m, 1 H), 2.20-1.88 (m, 8 H), 1.86-0.95 (m, 16 H), 0.88,0.67 (2 br loops, 3 H). MS(ESI–) m/z: 613 $(M-H)^-$

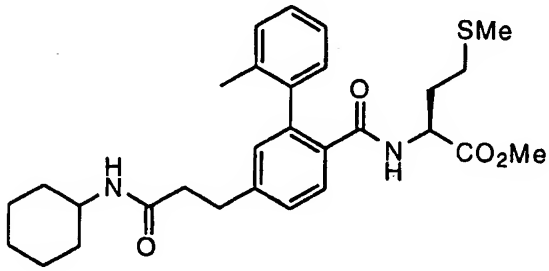
12675



Example 1139

N-[4-(N-Cyclohexylaminocarbonylethyl)-2-(2-methylphenyl)benzoyl]methionine lithium salt

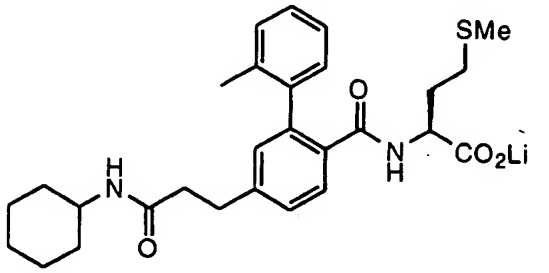
12680



Example 1139 A

N-[4-(N-Cyclohexylaminocarbonylethyl)-2-(2-methylphenyl)benzoyl]methionine lithium salt

The procedures descriped in the Example 403E and 403F were used here to convert 12685 intermediate 1144C (127 mg) to the title methyl ester (141 mg, 83%). ^{1}HNMR (300 MHz, $CDCl_3$) δ 7.89 (2 d's, 1 H), 7.32-7.24 (m, 4 H), 7.95 (br d, 1 H), 7.03 (br s, 1 H), 5.86 (br d, 1 H), 5.16 (m, 1 H), 4.62 (m, 1 H), 3.75 (m, 1 H), 3.02 (t, 2 H), 2.45 (t, 2 H), 2.20-2.00 (m, 8 H), 1.92-0.97 (m, 12 H).

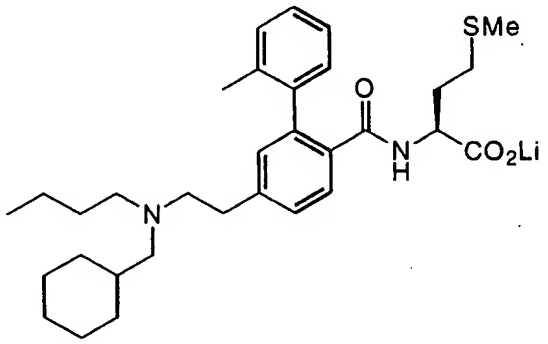


12690

Example 1139B

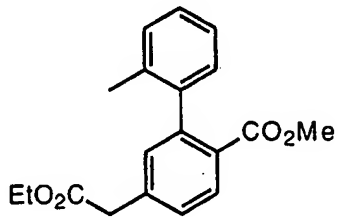
N-[4-(N-Cyclohexylaminocarbonylethyl)-2-(2-methylphenyl)benzoyl]methionine lithium salt

The procedure descriped in the Example 403I was used here to convert the intermediate 1139A (134 mg) to the title lithium salt (121 mg, 93%). ^{1}H NMR (300 MHz, dmso-d_6) δ 7.67 (d, 1 H), 7.45 (d, 1 H), 7.27-7.08 (m, 5 H), 6.97 (m, 1 H), 6.88 (m, 1 H), 3.66 (m, 1 H), 2.85 (t, 2 H), 2.36 (t, 2 H), 2.00-1.90 (m, 8 H), 1.88-0.98 (m, 12 H). MS(ESI–) m/z: 495 $(M-H)^-$.



Example 1140

N-[4-(N-cyclohexylmethyl-N-butylaminoethyl)-2-(2-methylphenyl)benzoyl]methionine lithium salt

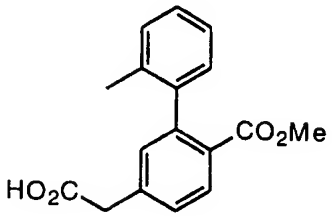


Example 1140A

Methyl 4-(Ethoxycarbonylmethyl)-2-(2-methylphenyl)benzoate

A solution of intermediate 1178D (397 g, 1.24 mmol), palladium(II) acetate (22 mg), 1,3-bis(diphenylphosphino)propane (42 mg), N,N–diisopropylethylamine (0.5 mL) in ethanol (1 mL) and DMF (5 mL) was stirred at 80 °C under carbon monoxide balloon for 4 hours. The reaction mixture was then partitioned between ethyl acetate (80 mL) and water (20 mL). The organic layer was washed with water (2 X 20 mL), brine (20 mL), dried over anhydrous magnesium sulfate, filtered and concentrated. The residue was purified by column chromatography with 5% ethyl acetate in hexane to give the title compound (233 mg, 58%). ^{1}HNMR (300 MHz, $CDCl_3$) δ 7.94 (d, 1 H), 7.35 (dd, 1 H), 7.30-7.17 (m, 3

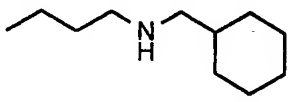
H), 7.16 (d, 1 H), 7.07 (br d, 1 H), 4.16 (q, 2 H), 3.67 (s, 2 H), 3.61 (s, 3 H), 2.06 (s, 3 H), 1.25 (t, 3 H). MS(CI/NH_3) m/z: 330 $(M+NH_4)^+$.



Example 1140B

Methyl 4-(Carboxymethyl)-2-(2-methylphenyl)benzoate

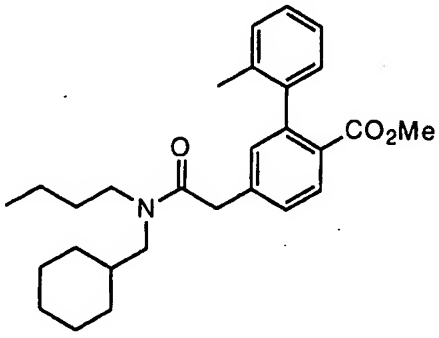
To the solution of intermediate 1140A (213 mg, 0.682 mmol) in methanol (3 mL) was added NaOH (0.979 M in water, 0.697 mL). After 2 hours, the reaction mixture was acidified with HCl (1.0 M, 1 mL), and was then partitioned between ethyl acetate (80 mL) and water (20 mL). The organic layer was washed with water (2 X 20 mL), brine (20 mL), dried over anhydrous magnesium sulfate, filtered and concentrated. The residue was used witout further purification.



Example 1140C

N-Butylcyclohexymethylamine

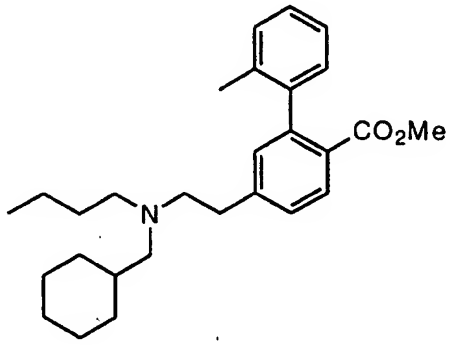
The procedures descriped in the Example 1178E and 1178F were used here to convert cyclohexylacetyl chloride (1.47 g, 10 .0 mmol) and butylamine to the title amine in 85% yield. The amine was not purified before it was used.



Example 1140D

Methyl 4-(N-Cyclohexylmethyl-N-butylaminocarbonylmethyl)-2-(2-methylphenyl)benzoate

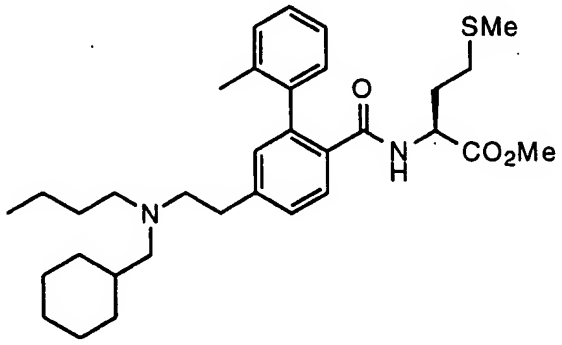
The procedure described in example 1144C was used here to combine intermediate 1140B (311 mg, 1.10 mmol) and intermediate 1140C (205 mg) to give the title compound (247 mg, 52%). ^{1}HNMR (300 MHz, $CDCl_3$) δ 7.94 (d, 1 H), 7.33 (M, 1 H), 7.25-7.15 (m, 3 H), 7.13,7.11 (2 d's, 1 H), 7.05 (m, 1 H), 3.76,3.75 (2 s's, 2 H), 3.60 (s, 3 H), 3.35-3.05 (m, 4H), 2.05,2.04 (2 s's, 3 H), 1.80-1.10 (m, 15 H), 0.91,0.89 (2 t's, 3 H). MS(CI/NH_3) m/z: 436 $(M+H)^+$.



Example 1140E

Methyl 4(N–Cyclohexylmethyl-N-butylaminoethyl)-2-(2-methylphenyl)benzoate

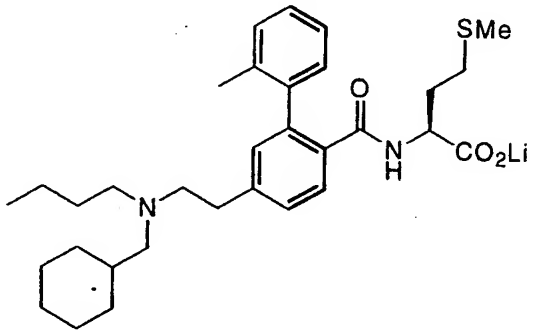
A solution of intermediate 1140D (118 mg, 0.271 mmol) and borane (1.0 M in THF, 0.54 mL) in THF was reluxed for 15 hours. Methanol (0.5 mL) was added dropwisly to the reaction, followed by concentrated HCl (0.5 mL), and the mixture was heated at 60 °C for 1 hour. The it was cooled to room temperature, The reaction mixture was adjusted to pH about 12-14 with sodium carbonate (2.0 M in water). The reaction mixture was then partitioned between ethyl acetate (50 mL) and water (5 mL). The organic layer was washed with water (10 mL), brine (20 mL), dried over anhydrous magnesium sulfate, filtered and concentrated to give the intermediate amine 1140E. The amine was used without further purification. ^{1}HNMR (300 MHz, $CDCl_3$) δ 7.90 (d, 1 H), 7.28-7.17 (m, 4 H), 7.05 (m, 2 H), 3.60 (s, 3 H), 2.75 (m, 2 H), 2.66 (m, 2 H), 2.40 (t, 2 H), 2.19 (d, 2 H), 2.06 (s, 3 H), 1.80-1.10 (m, 15 H), 0.88 (t, 3 H). MS(CI/NH_3) m/z: 422 $(M+H)^+$.



Example 1140F

N-[4-(N-Cyclohexylmethyl-N-butylaminoethyl)-2-(2-methylphenyl)benzoyl]methionine Methyl Ester

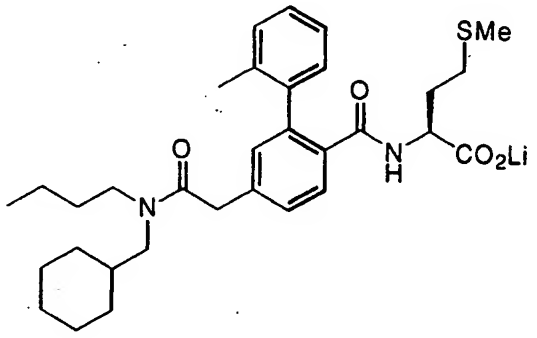
The procedures descriped in the Example 403E and 403F were used here to convert the above intermediate amine 1140E to the title methyl ester (113 mg, 76%, 3 steps from 1140D). ^{1}HNMR (300 MHz, $CDCl_3$) δ 7.90 (2 d's, 1 H), 7.34-7.18 (m, 5 H), 7.01 (s, 1 H), 5.87 (br d, 1 H), 4.62 (m, 1 H), 3.65 (s, 3 H), 2.75 (m, 2 H), 2.66 (m, 2 H), 2.41 (t, 2 H), 2.20 (d, 2 H), 2.19-1.98 (m, 8 H), 1.87 (m, 1 H), 1.80-1.10 (m, 16 H), 0.88 (t, 3 H). MS(CI/NH_3) m/z: 553 $(M+H)^+$.



Example 1140G

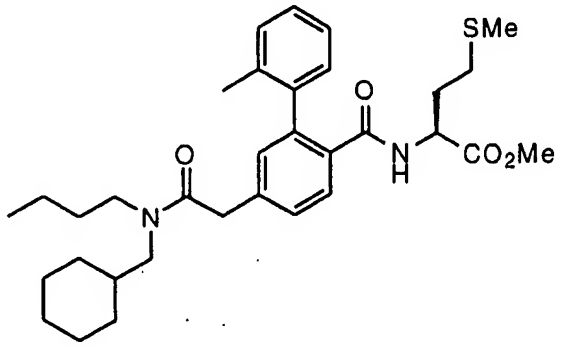
N-[4-(N-cyclohexylmethyl-N-butylaminoethyl)-2-(2-methylphenyl)benzoyl]methionine lithium salt

The procedure descriped in the Example 403I was used here to convert the intermediate 1140F (107 mg) to the title lithium salt (91 mg, 87%). ^{1}H NMR (300 MHz, dmso-d_6) δ 7.51 (d, 1 H), 7.33-7.13 (m, 5 H), 7.05 (br s, 1 H), 6.95 (m, 1 H), 3.71 (m, 1 H), 2.76 (m, 2 H), 2.67 (m, 2 H), 2.42 (t, 2 H), 2.21 (d, 2 H), 2.10-1.82 (m, 8 H), 1.80-1.10 (m, 17 H), 0.88 (t, 3 H). MS(ESI–) m/z: 537 $(M-H)^-$.



Example 1141

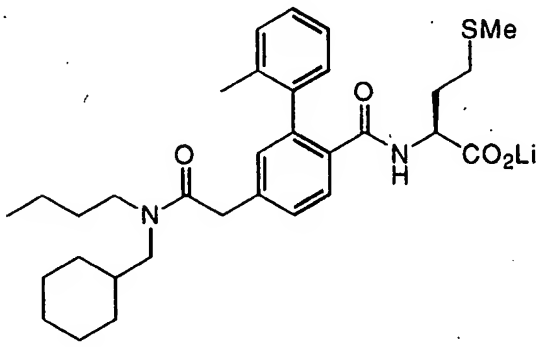
N-[4-(N-Cyclohexylmethyl-N-butylaminocarbonylmethyl)-2-(2-methylphenyl)benzoyl]methionine lithium salt



Example 1141A

N-[4-(N-Cyclohexylmethyl-N-butylaminocarbonylmethyl)-2-(2-methylphenyl)benzoyl]methionine Methyl Ester

The procedures descriped in the Example 403E and 403F were used here to convert the intermediate 1140D (101 mg) to the title methyl ester (127 mg, 97%). ^{1}HNMR (300 MHz, $CDCl_3$) δ 7.92 (m, 1 H), 7.37-7.22 (m, 4 H), 7.19 (m, 1 H), 7.11 (br d, 1 H), 5.88 (br d, 1 H), 4.61 (m, 1 H), 3.76,3.75 (2 s's, 2 H), 3.65 (s, 3 H), 3.37-2.04 (m, 4 H), 2.00-1.97 (m, 8 H), 1.95-1.10 (m, 17 H), 0.92,0.88 (2 t's, 3 H). MS(CI/NH_3) m/z: 567 $(M+H)^+$.

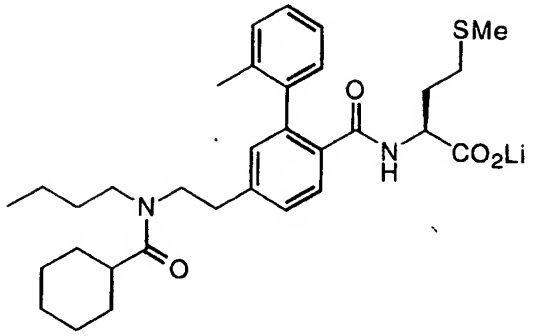


Example 1141B

N-[4-(N-Cyclohexylmethyl-N-butylaminocarbonylmethyl)-2-(2-methylphenyl)benzoyl]methionine lithium salt

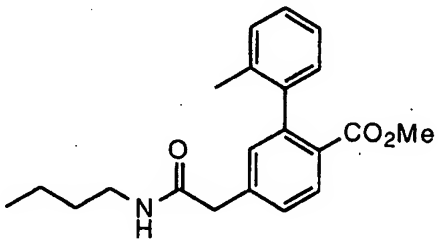
The procedure descriped in the Example 403I was used here to convert the intermediate 1141A (119 mg) to the title lithium salt (102 mg, 86%). ^{1}H NMR (300 MHz, dmso-d_6) δ 7.48 (2 d's, 1 H), 7.30 (m, 1 H), 7.25-7.08 (m, 4 H), 7.03 (br s, 1 H), 5.95 (m, 1 H), 3.74,3.72 (2 s's, 2 H), 3.69 (m, 1 H), 3.23 (t, 2 H), 3.11 (m, 2 H), 2.20-1.90

(m, 8 H), 1.85 (m, 1 H),), 1.79-1.00 (m, 17 H), 0.86,0.83 (2 t's, 3 H). MS(ESI–) m/z: 551 $(M-H)^-$.



Example 1142

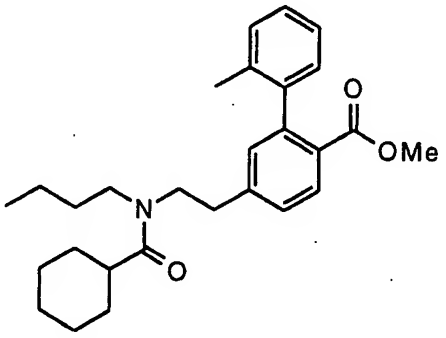
N-[4-(N-Cyclohexanoyl-N-butylaminoethyl)-2-(2-methylphenyl)benzoyl]methionine lithium salt



Example 1142A

Methyl 4-(N-Butylaminocarbonylmethyl)-2-(2-methylphenyl)benzoate

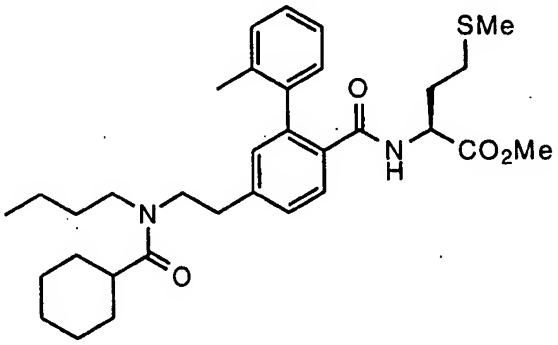
The procedure described in example 1144C was used here to combine intermediate 1140B (200 mg, 0.70 mmol) and butylamine to give the title compound (171 mg, 69%). ^{1}HNMR (300 MHz, $CDCl_3$) δ 7.95 (d, 1 H), 7.34 (dd, 1 H), 7.30-7.17 (m, 3 H), 7.13 (d, 1 H), 7.05 (d, 1 H), 5.36 (m, 1 H), 3.61 (s, 3 H), 3.60 (s, 2 H), 3.24 (q, 1 H), 2.07 (s, 3 H), 1.42 (m, 2 H), 1.27 (m, 2 H), 0.88 (t, 3 H).



Example 1142B

Methyl N-[4-(N-Cyclohexanoyl-N-butylaminoethyl)-2-(2-methylphenyl)benzoate

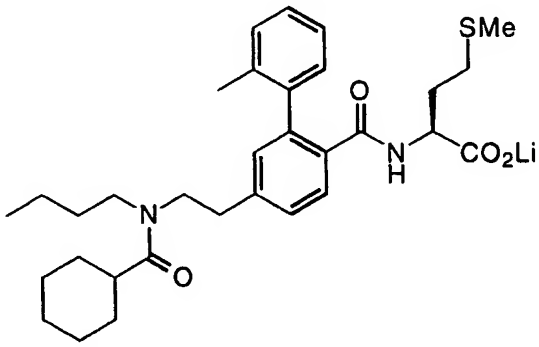
The procedures described in 1143B was used here to convert 1142A (102 mg, 0.36 mmol) to the title compound (137 mg, 87%). ^{1}HNMR (300 MHz, $CDCl_3$) δ 7.92 (2 d's, 1 H), 7.30-7.17 (m, 4 H), 7.05 (m, 2 H), 3.61 (2 s's, 3 H), 3.52 (m, 2 H), 3.07,3.06 (2 t's, 2 H), 2.90 (t, 2 H), 2.37 (m, 1 H), 2.07,2.04 (2s's, 3 H), 2.00-1.15 (m, 14 H), 0.92,0.90 (2 t's, 3 H). MS(CI/NH_3) m/z: 436 $(M+H)^+$.



Example 1142C

N-[4-(N-Cyclohexanoyl-N-butylaminoethyl)-2-(2-methylphenyl)benzoyl]methionine Methyl Ester

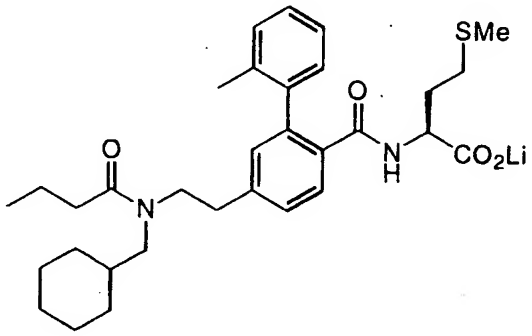
The procedures descriped in the Example 403E and 403F were used here to convert the above intermediate 1142B (130 mg) to the title methyl ester (112 mg, 66%). ^{1}HNMR (300 MHz, $CDCl_3$) δ 7.91 (2 d's, 1 H), 7.37-7.15 (m, 5 H), 7.06,6.99 (2 br s's, 1 H), 6.90 (br d, 1 H), 4.61 (m, 1 H), 3.66,2.65 (2 s's, 3 H), 3.52 (m, 2 H), 3.19,2.92 (2 m's, 4 H), 2.30-2.00 (m, 9 H), 1.86 (m, 1 H), 1.80,1.10 (m, 15 H), 0.94,0.91 (2 t's, 3 H). MS(CI/NH_3) m/z: 567 $(M+H)^+$.



Example 1142D

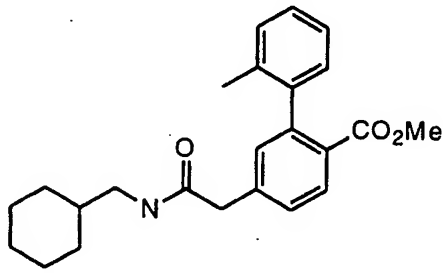
N-[4-(N-Cyclohexanoyl-N-butylaminoethyl)-2-(2-methylphenyl)benzoyl]methionine lithium salt

The procedure descriped in the Example 403I was used here to convert the intermediate 1142C (103 mg) to the title lithium salt (99 mg, 97%). ^{1}H NMR (300 MHz, dmso-d_6) δ δ 7.48 (2 d's, 1 H), 7.31-6.86 (m, 7 H), 3.63 (m, 1 H), 3.48 (m, 2 H), 3.10,2.95 (2 m's, 2 H), 2.82 (2 t's, 2 H), 2.25-1.90 (m, 9 H), 1.80 (m, 1 H), 1.75-1.07 (m, 15 H), 0.84,0.80 (2 t's, 3 H). MS(ESI–) m/z: 551 $(M-H)^-$.



Example 1143

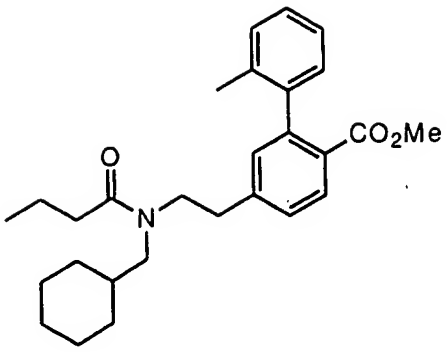
N-[4-(N-Cyclohexylmethyl-N-butanoylaminoethyl)-2-(2-methylphenyl)benzoyl]methionine lithium salt



Example 1143A

Methyl 4-(N-Cyclohexylmethylaminocarbonylmethyl)-2-(2-methylphenyl)benzoate

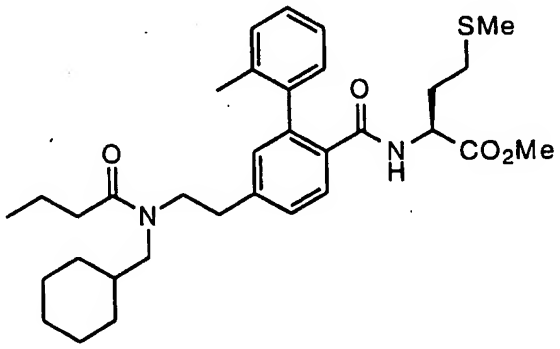
The procedure described in example 1144C was used here to combine intermediate 1140B (301 mg, 1.05 mmol) and cyclohexylmethylamine to give the title compound (266 mg, 67%). ^{1}HNMR (300 MHz, $CDCl_3$) δ 7.97 (d, 1 H), 7.35 (dd, 1 H), 7.27-7.17 (m, 3 H), 7.15 (d, 1 H), 7.05 (d, 1 H), 5.41 (m, 1 H), 3.62 (2 overlapped s's, 5 H), 3.07 (t, 2 H), 2.06 (s, 3 H), 1.85-0.87 (m, 11 H). MS(CI/NH_3) m/z: 380 $(M+H)^+$.



Example 1143B

Methyl 4-(N-Cyclohexylmethyl-N-butanoylaminoethyl)-2-(2-methylphenyl)benzoate

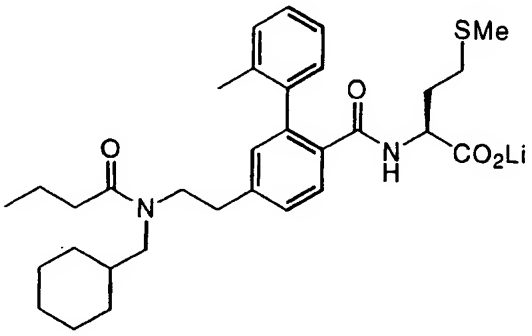
To a solution of intermediate 1143A (108 mg, 0.285 mmol) in THF (2 ML) was added borane (1.0 M in THF, 0.5 mL), and the reaction mixture was stirred at room temperature for 7 hours. Methanol (0.5 mL) was added dropwisly to the reaction, followed by concentrated HCl (0.5 mL), and the mixture was heated at 60 °C for 1 hour. Then it was cooled to room temperature, and was adjusted to pH about 12-14 with sodium carbonate (2.0 M in water). The reaction mixture was then partitioned between ethyl acetate (50 mL) and water (5 mL). While still in the separatory funnel, butyryl chloride (0.5 mL) was added to the organic layer, followed by additon of sodium bicarbonate (saturated in water, 5 mL), and the mixture was well shaked. The mixture was washed with NaOH (1.0 M, 10 mL), water (2 X 10 mL), brine (10 mL), dried over anhydrous magnesium sulfate, filtered and concentrated. The residue was purified by column chromatography with 20% ethyl acetate in hexane to give the title compound (to give the title amine (113 mg, 91%). ^{1}HNMR (300 MHz, $CDCl_3$) δ 7.94 (2d'd, 1 H), 7.31-7.18 (m, 4 H), 7.10-7.02 (m, 2 H), 3.62,3.61 (2 s's, 3 H), 3.52 (m, 2 H), 3.00-2.85 (m, 4 H), 2.26,2.18 (2 t's, 2 H), 2.06,2.05 (2 s's, 3 H), 1.80-0.80 (m, 13 H), 0.94,0.91 (2 t's, 3 H). MS(CI/NH_3) m/z: 436 $(M+H)^+$.



Example 1143C

N-[4-(N-Cyclohexylmethyl-N-butanoylaminoethyl)-2-(2-methylphenyl)benzoyl]methionine Methyl Ester

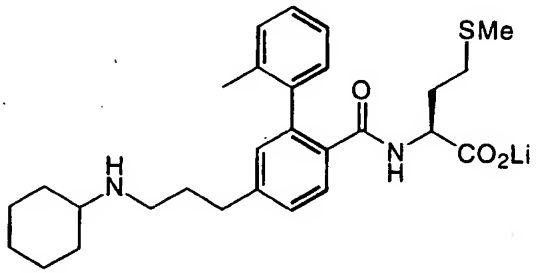
The procedures descriped in the Example 403E and 403F were used here to convert the above intermediate 1143B (130 mg, 0.300 mmol) to the title methyl ester (112 mg, 66%). ^{1}HNMR (300 MHz, $CDCl_3$) δ 7.90 (m, 1 H), 7.35-7.21 (m, 4 H), 7.19 (m, 1 H), 7.03 (br d, 1 H), 5.89 (br d, 1 H), 4.61 (m, 1 H), 3.65 (s, 3 H), 3.52 (m, 2 H), 3.30,3.07 (2 m's, 2 H), 2.90 (t, 2 H), 2.40-1.97 (m, 10 H), 1.90-1.10 (m, 15 H), 0.92,0.90 (2 t's, 3 H). MS(CI/NH_3) m/z: 567 $(M+H)^+$.



Example 1143D

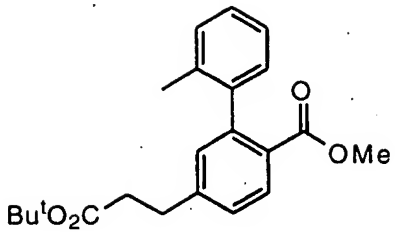
N-[4-(N-Cyclohexylmethyl-N-butanoylaminoethyl)-2-(2-methylphenyl)benzoyl]methionine lithium salt

The procedure descriped in the Example 403I was used here to convert the intermediate 1143C (104 mg) to the title lithium salt (95 mg, 100%). ^{1}H NMR (300 MHz, dmso-d_6) δ 7.48 (2 d's, 1 H), 7.31-7.10 (m, 5 H), 7.10-6.87 (m, 2 H), 3.66 (m, 1 H), 3.57-3.39 (m, 2 H), 3.22,3.09 (2 m's, 2 H), 2.85,2.79 (2 t's, 2 H), 2.40,2.25 (2 m's, 2 H), 2.20-1.90 (m, 8 H), 1.83 (m, 1 H), 1.75-1.06 (m, 14 H), 0.87,0.85 (2 t's, 3 H). MS(ESI–) m/z: 551 $(M-H)^-$.



Example 1144

N-[4-(N-Cyclohexylpropyl)-2-(2-methylphenyl)benzoyl]methionine lithium salt

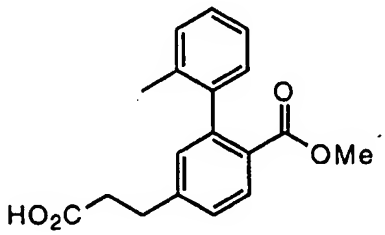


Example 1144A

Methyl 4-(tert-Butoxycarbonylethyl)-2-(2-methylphenyl)benzoate

To a solution of (t-butoxycarbonylmethyl)triphenylphosphonium bromide (10.98 g, 24.0 mmol) in THF (150 mL) at 0 °C was added potassium t-butoxide (1.0 M in THF, 24 mL) over 5 min. After 2 h, the aldehyde from example 1171A (20 mmol) in THF (10 mL) was added slowly over 5 min., and the reaction was further stirred for 30 min. The reaction mixture was diluted with hexane (200 mL), and the resulting muddy mixture was filtered through silica gel (200 g), rinsed with ether, and concentrated to give an intermediate olefin. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.97 (d, 1 H), 7.59 (d, 1 H), 7.54 (dd, 1 H), 7.37 (d, 1 H), 7.30-7.27 (m, 3 H), 7.06 (d, 1 H), 6.44 (d, 1 H), 3.61 (s, 3 H), 2.06 (s, 3 H), 1.52 (s, 9 H). MS(CI/NH_3) m/z: 353 $(M+H)^+$, 370 $(M+NH_4)^+$.

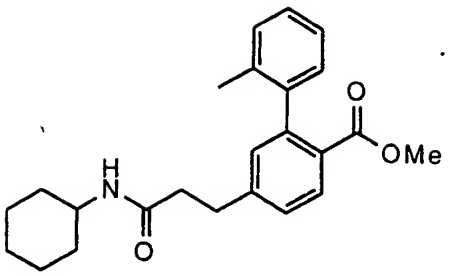
That intermediate was mixed with palladium on carbon (10%, 2.0 g) in ethanol (30 mL), and was stirred under a hydrogen balloon overnight. The mixture was then filtered through Celite™ (5 g), and the filtrate was concentrated. The residue was then redesolved in ether (100 mL) and the solution was filtered through silica gel (30 g). Concentration of the filtrate afforded the title compound (7.27 g, 99% for 2 steps). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.91 (d, 1H), 7.28-7.15 (m, 4 H), 7.07-7.03 (m, 2 H), 3.60 (s, 3 H), 2.97 (t, 2 H), 2.57 (t, 2 H), 2.05 (s, 3 H), 1.40 (s, 9 H). MS(CI/NH_3) m/z: 355 $(M+H)^+$, 372 $(M+NH_4)^+$.



Example 1144B

Methyl 4-(2-Carboxyethyl)-2-(2-methylphenyl)benzoate

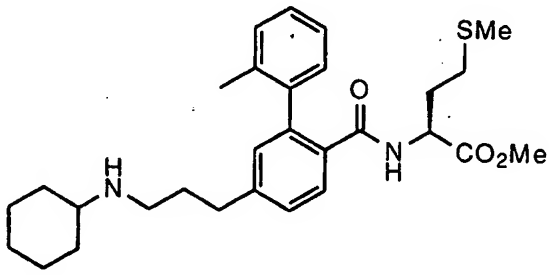
A solution of intermediate 1144A (5.00 g) in trifluoroacetic acid (20 mL) and methyl sulfide (3 mL) was stirred at room temperature for 7 hours. Sovlent was then evaporated to give an off-white solid, which was used without further purification.



Example 1144C

Methyl 4-(2-Cyclohexylcarbomoylethyl)-2-(2-methylphenyl)benzoate

To a solution of intermediate 1144B (150 mg, 0.50 mmol), oxallyl chloride (2.0 M in DCM, 0.5 mL) in DCM (2 mL) was added a small drop of DMF. After 2 hours at room temperature , the reaction was concentrated to drynees, and redeolved in DCM (3 mL). To it was added cyclohexylamine (99 mg, 1 mmol) and triethylamine (100 mg, 1 mmol). After 15 min., HCl (1.0 M in ether, 2.0 mL) was added to the reaction mixture, and it was filtered through silica gel (5 g). The residue after concentration of the filtrate was purified by column chromatography with 20% ethyl acetate in hexane to give the title compound (152 mg, 80%). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.90 (d, 1 H), 7.28-7.15 (m, 4 H), 7.07-7.02 (m, 2 H), .5.16 (m, 1 H), 3.72 (m, 1 H), 3.60 (s, 3H), 3.02 (t, 2 H), 2.45 (t, 2 H), 2.05 (s, 3 H), 1.85 (m, 2 H), 1.70-1.55 (m, 3 H), 1.40-0.95 (m, 6 H). MS(CI/NH_3) m/z: 380 $(M+H)^+$, 397 $(M+NH_4)^+$.



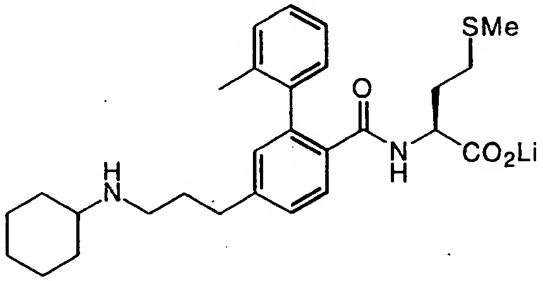
Example 1144D

N-[4-(N-Cyclohexylpropyl)-2-(2-methylphenyl)benzoyl]methionine

A solution of intermediate 1144C (150 mg, 0.40 mmol) and borane (1.0 M in THF, 1.0 mL) in THF (1 mL) was reluxed for 15 hours. Methanol (0.5 mL) was added dropwisly to the reaction, followed by concentrated HCl (0.5 mL), and the mixture was heated at 60 °C for 1 hour. The reaction mixture was cooled to room temperature, and was adjusted to pH about 12-14 with sodium carbonate (2.0 M in water). The reaction mixture was then partitioned between ethyl acetate (50 mL) and water (5 mL). The organic layer was washed with water (10 mL), brine (20 mL), dried over anhydrous magnesium sulfate, filtered and

concentrated to give the intermediate amine. The amine was used without further purification. MS(CI/NH_3) m/z: 366 $(M+H)^+$.

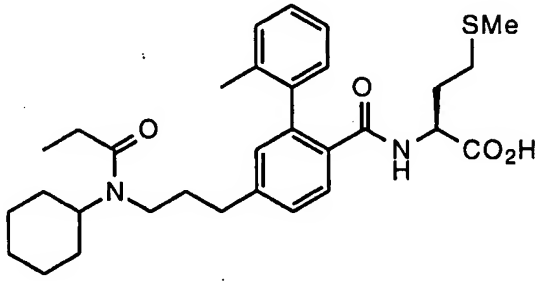
The procedures described in the Example 403E and 403F were used here to convert the above intermediate amine to the title methyl ester (58%, 3 steps).



Example 1144E

N-[4-(N-Cyclohexylpropyl)-2-(2-methylphenyl)benzoyl]methionine lithium salt

The procedure described in the Example 403I was used here to convert the intermediate 1144D (121 mg) to the title lithium salt (107 mg, 100%). ^{1}H NMR (300 MHz, dmso-d_6) δ 7.45 (d, 1 H), 7.27-7.08 (m, 4 H), 7.02-6.93 (m, 2 H), 6.90 (m, 1 H), 3.80 (m, 1 H), 3.65 (m, 1 H), 3.30 (m, 2 H), 2.64 (t, 2 H), 2.20-1.80 (m, 10 H), 1.80-1.45 (m, 7 H), 1.30-0.88 (m, 6 H). MS(ESI–) m/z: 481 $(M-H)^-$.

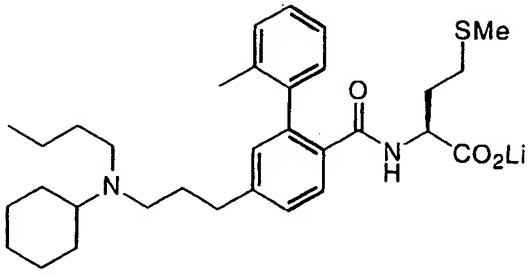


Example 1145

N-[4-(N-Cyclohexyl-N-propanoylaminopropyl)-2-(2-methylphenyl)benzoyl]methionine

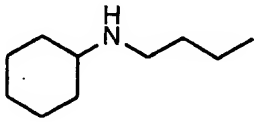
To s stirred mixture of 1144E (70 mg, 0.14 mmol) in THF (1 mL) and saturated aqueous sodium bicarbonate (1 mL) was added propionyl chloride (0.10 mL). After 10 min, the reaction mixture was adjusted to pH 4-5, and it was then partitioned between ethyl acetate (50 mL) and water (5 mL). The organic layer was washed with water (10 mL), brine (10 mL), dried over anhydrous magnesium sulfate, filtered and concentrated. The residue was heated at 60 °C under high vacuum for 5 hours to give the title compound (59 mg, 78%). ^{1}H NMR (300 MHz, dmso-d_6) δ 7.47 (m, 1 H), 7.32-6.97 (m, 7 H), 4.25 (m, 1 H),

3.57 (m, 1 H), 3.35 (m, 2 H), 2.80-2.60 (m, 2 H), 2.30-1.85 (m, 12 H), 1.85-1.45 (m, 7 H), 1.30-0.88 (m, 9 H). MS(ESI–) m/z: 537 $(M-H)^-$.



Example 1146

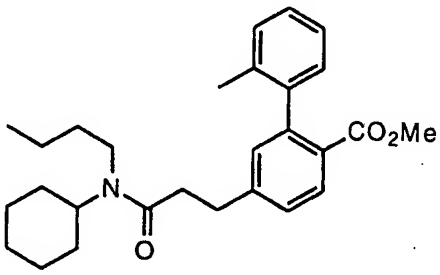
N-[4-(N-Cyclohexyl-N-butylaminopropyl)-2-(2-methylphenyl)benzoyl]methionine lithium salt



Example 1146A

N–Butylcyclohexaylamine

The procedures descriped in the Example 1178E and 1178F were used here to convert butyric chloride and cyclohexylamine to the title amine in 86% yield. ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.62 (t, 2 H), 2.41 (m, 1 H), 1.95-1.00 (m, 15 H), 0.92 (t, 3 H). MS(CI/NH_3) m/z: 156 $(M+H)^+$.

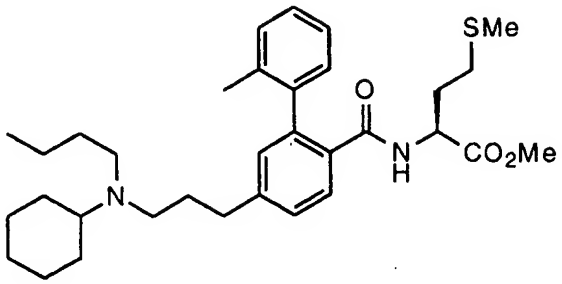


Example 1146B

Methyl N-[4-(N-Cyclohexyl-N-butylaminopropyl)-2-(2-methylphenyl)benzoate

The procedure descriped in the Example 1144C was used here to convert the intermediate 1144B (298 mg) and N–butylcyclohexylamine (intermediate 1146A, 310 mg, 2.0 mmol) to the title methyl ester (233 mg, 54%). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.90 (2 d's, 1 H), 7.30-7.15 (m, 4 H), 7.07 (m, 2 H), 4.25 (m, 1 H), 3.60 (s, 3 H), 3.18 (m, 1

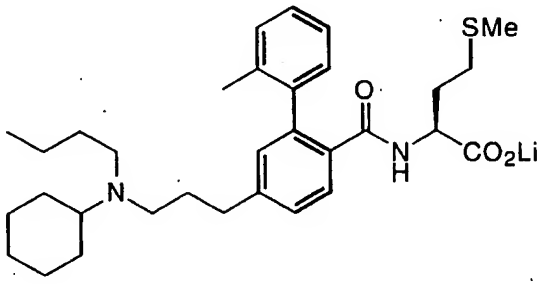
H), 3.05 (m, 3 H), 2.62 (m, 2 H), 2.06 (2s's, 3 H), 1.85-1.05 (m, 14 H), 0.90 (2 t's, 3 H). MS(CI/NH_3) m/z: 436 $(M+H)^+$.



Example 1146C

N-[4-(N-Cyclohexyl-N-butylaminopropyl)-2-(2-methylphenyl)benzoyl]methionine Methyl Ester

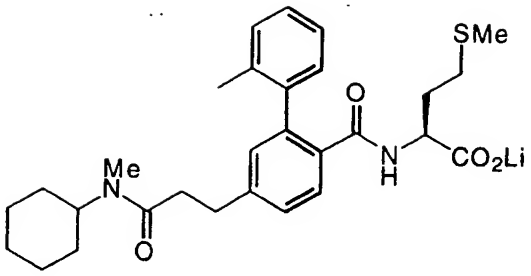
The procedure descriped in the Example 1144C was used here to convert the intermediate 1146B (230 mg) to the title methyl ester (184 mg, 63%). ^1H NMR (300 MHz, $CDCl_3$) δ 7.90 (2 d's, 1 H),), 7.35-7.19 (m, 4 H), 7.03 (m, 1 H), 5.89 (m, 1 H), 4.62 (m, 1 H), 3.66 (s, 3 H), 3.05 (m, 1 H), 2.66 (t, 2 H), 2.46 (t, 2 H), 2.41 (t, 2 H), 2.20-2.00 (4 s's, 6 H), 2.05 (m, 2 H), 1.90-1.00 (m, 18 H), 0.90 (t, 3 H). MS(CI/NH_3) m/z: 553 $(M+H)^+$.



Example 1146D

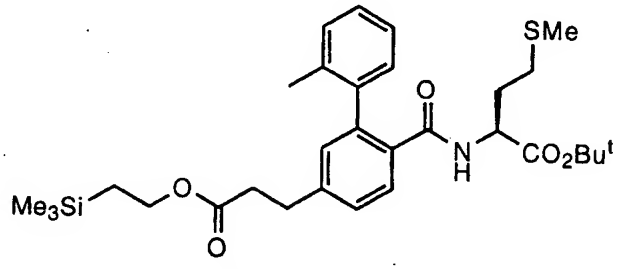
N-[4-(N-Cyclohexyl-N-butylaminopropyl)-2-(2-methylphenyl)benzoyl]methionine lithium salt

The procedure descriped in the Example 403I was used here to convert the intermediate 1146C (179 mg) to the title lithium salt (153 mg, 81%). ^1H NMR (300 MHz, dmso-d_6) δ 7.46 (m, 1 H), 7.35-7.08 (m, 4 H), 7.07-6.90 (m, 2 H), 3.70 (m, 1 H), 3.05 (m, 1 H), 2.64 (t, 2 H), 2.37 (m, 4 H), 2.20-1.90 (m, 8 H), 1.90-0.95 (m, 18 H), 0.85 (t, 3 H). MS(ESI–) m/z: 537 $(M-H)^-$.



Example 1147

N-[4-(N-Cyclohexyl-N-methylaminocarbonylethyl)-2-(2-methylphenyl)benzoyl]methionine lithium salt

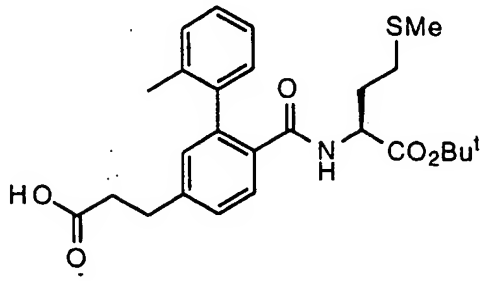


Example 1147A

[4-(2-Trimethylsilylethoxycarbonylethyl)-2-(2-methylphenyl)benzoyl]methionine tert–Butyl Ester

A solution of intermediate 1144A (875 mg, 2.38 mmol) and LiOH (5.3 M in water, 2.0 mL) in methanol (5 mL) was refluxed 15 hours. The mixture was then acidified with concentrated HCl (1 mL) to pH<3. The reaction mixture was then partitioned between ethyl acetate (100 mL) and brine (20 mL). The organic layer was dried over anhydrous magnesium sulfate, filtered and concentrated. The resulting white solid was desolved in DMF (10 mL). To it was added 2-trimethylsilylethanol (0.357 mL, 2.49 mmol), and 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide (545 mg, 2.84 mmol), and DMAP (10 mg). After 2 hours, triethylamine (809 mg, 8.0 mmol) L-methionine tert-butyl ester hydrochloride (725 mg, 3.0 mmol), 1-hydroxybenzotriazole (400 mg, 3.0 mmol) and 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide (577 mg, 3.0 mmol). After 15 hours at room temperature, the reaction mixture was partitioned between ethyl acetate (100 mL) and water (10 mL). The organic layer was washed with water (3 X 15 mL), brine (20 mL), dried over anhydrous magnesium sulfate, filtered and concentrated. The residue was purified by column chromatography with 10% ethyl acetate in hexane to give the title compound (859 mg, 68%). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.83 (2 d'd, 1 H), 7.33-7.15 (m, 5 H), 7.04 (br s, 1 H), 5.85 (br d, 1 H), 4.50 (m, 1 H), 4.16 (t, 2 H), 3.00 (t, 2 H), 2.63 (t, 2 H),

2.17,2.07,2.03,2.02 (4 s's, 6 H), 2.00 (m, 2 H), 1.80 (m, 1 H), 1.55 (m, 1 H), 1.40 (s, 9 H), 0.95 (t, 2 H), 0.03 (s, 9 H). MS(CI/NH_3) m/z: 572 $(M+H)^+$.

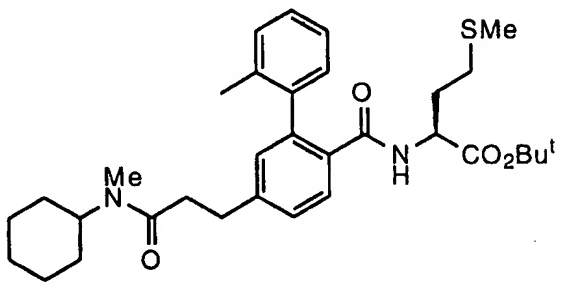


13070

Example 1147B

[4-(2-Carboxyethyl)-2-(2-methylphenyl)benzoyl]methionine tert–Butyl Ester

A solution of intermediate 1147A (841mg, 1.57 mmol), tetrabutylammomium fluoride (820 mg, 3.14 mmol) in DMF (5 mL) was stirred overnight. The reaction mixture
13075 was then adjusted to pH 3-5, and was partitioned between ethyl acetate (100 mL) and water (20 mL). The organic layer was washed with water (2 X 20 mL), brine (20 mL), dried over anhydrous magnesium sulfate, filtered and concentrated to give the title compound. The crude product was used without further purification. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.83 (2 d'd, 1 H), 7.33-7.15 (m, 5 H), 7.05 (br s, 1 H), 5.87 (m, 1 H), 4.50 (m, 1 H), 3.01 (t,
13080 2 H), 2.71 (t, 2 H), 2.20-2.02 (4 s's, 6 H), 2.00 (m, 2 H), 1.80 (m, 1 H), 1.59 (m, 1 H), 1.40 (s, 9 H). MS(CI/NH_3) m/z: 472 $(M+H)^+$.

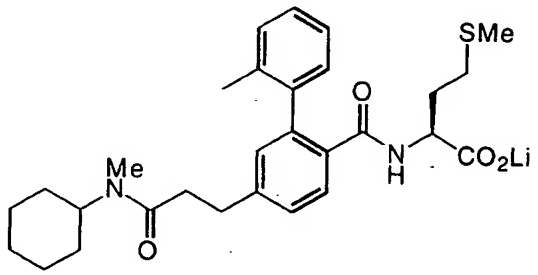


Example 1147C

13085 N-[4-(N-Cyclohexyl-N-methylaminocarbonylethyl)-2-(2-methylphenyl)benzoyl]methionine tert-Butyl Ester

A solution of intermediate 1147B (50 mg, 0.115 mmol), triethylamine (100 mg), 1-hydroxybenzotriazole (31 mg, 0.23 mmol), 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide (44 mg, 0.23 mmol), and N-methylcyclohexylamine (26 mg, 0.23 mmol) in DMF (2 mL)
13090 was stirred 15 hours at room temperature. The reaction mixture was then partitioned between ethyl acetate (50 mL) and water (5 mL). The organic layer was washed with water (3 X 5 mL), brine (5 mL), dried over anhydrous magnesium sulfate, filtered and

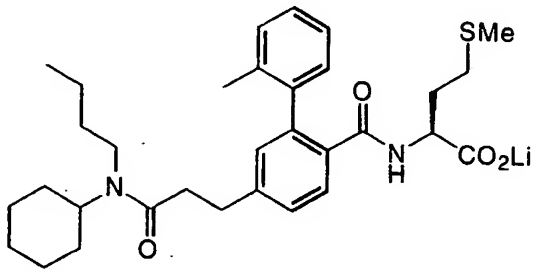
concentrated. The residue was purified by column chromatography with 40% ethyl acetate in hexane to give the title compound (44 mg, 68%). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.84 (m, 1 H), 7.33-7.15 (m, 5 H), 7.05 (br s, 1 H), 5.84 (m, 1 H), 4.47 (m, 2 H), 3.02 (t, 2 H), 2.81,2.77 (2s's, 3 H), 2.62 (m, 2 H), 2.20-1.97 (m, 8 H), 1.90-1.25 (m, 12 H), 1.40 (s, 9 H). MS(CI/NH_3) m/z: 567 $(M+H)^+$.



Example 1147D

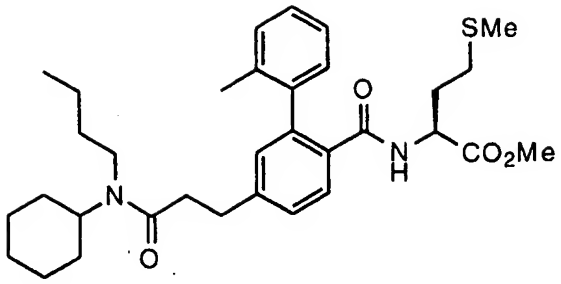
N-[4-(N-Cyclohexyl-N-methylaminocarbonylethyl)-2-(2-methylphenyl)benzoyl]methionine lithium salt

The intermediate 1147C (40 mg) was stirred with HCl (4.0 N in dioxane, 1.0 mL) in DCM (1 mL) at room temperature for 15 hours. Solvent was then evaporated, and the residue was desolved in acetonitrile (1 mL), treated with 1.1 equivalent of LiOH (1.0 M in water, 0.078 mL), and freeze-dried to give the title compound (37 mg, 100%). ^{1}HNMR (300 MHz, dmso-d_6) δ 7.44 (d, 1 H), 7.30 (m, 1 H), 7.25-7.08 (m, 4 H), 7.03 (m, 1 H), 6.87 (m, 1 H), 4.23 (m, 1 H), 3.66 (m, 1 H), 2.87 (m, 2 H), 2.74,2.66 (2s's, 3 H), 2.62 (m, 2 H), 2.20-1.90 (m, 8 H), 1.90-1.25 (m, 12 H). MS(ESI–) m/z: 509 $(M-H)^-$.



Example 1148

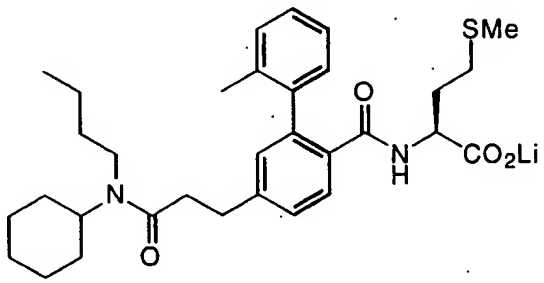
N-[4-(N-Cyclohexyl-N-butylaminocarbonylethyl)-2-(2-methylphenyl)benzoyl]methionine lithium salt



Example 1148A

N-[4-(N-Cyclohexyl-N-butylaminocarbonylethyl)-2-(2-methylphenyl)benzoyl]methionine Methyl ester

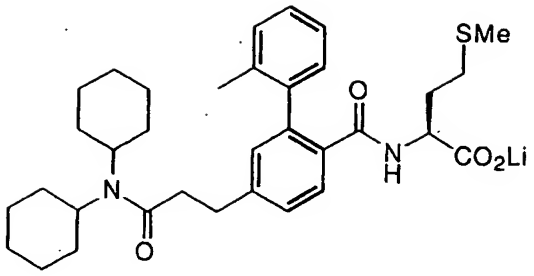
The procedures descriped in the Example 403E and 403F were used here to convert the intermediate 1146B (102mg) to the title methyl ester (117 mg, 90%). ^{1}HNMR (300 MHz, $CDCl_3$) δ 7.91 (2 d's, 1 H), 7.35-7.15 (m, 5 H), 7.06 (br s, 1 H), 6.88 (m, 1 H), 4.61 (m, 1 H), 3.49 (m, 1 H), 3.66 (s, 3 H), 3.20-3.00 (m, 4 H), 2.66-2.50 (m, 2 H), 2.20-2.00 (m, 8 H), 1.90-0.95 (m, 16 H), 0.91 (t, 3 H). MS(CI/NH_3) m/z: 566 $(M+H)^+$.



Example 1148B

N-[4-(N-Cyclohexyl-N-butylaminocarbonylethyl)-2-(2-methylphenyl)benzoyl]methionine lithium salt

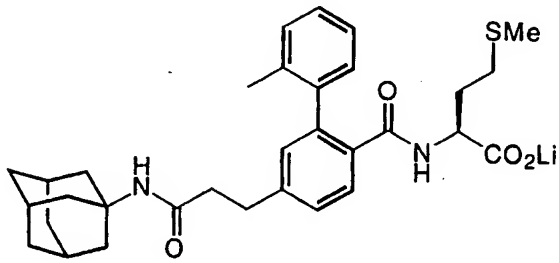
The procedure descriped in the Example 403I was used here to convert the intermediate 1148A (108 mg) to the title lithium salt (91 mg, 83%). ^{1}HNMR (300 MHz, dmso-d_6) δ 7.44 (d, 1 H), 7.27 (t, 1 H), 7.23-7.05 (m, 3 H), 7.04-6.91 (m, 2 H), 6.89 (d, 1 H), 4.07 (m, 1 H), 3.65 (m, 1 H), 3.06 (m, 2 H), 2.88 (m, 2 H), 2.65,2.57 (2 t't, 2 H), 2.20-1.90 (m, 8 H), 1.90-0.95 (m, 16 H), 0.84 (t, 3 H). MS(ESI–) m/z: 537 $(M-H)^-$.



Example 1149

N-[4-(N,N-dicyclohexylaminocarbonylethyl)-2-(2-methylphenyl)benzoyl]methionine lithium salt

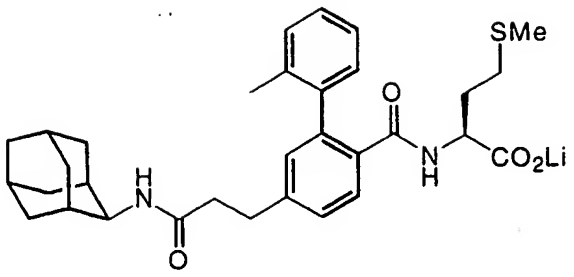
The procedures descriped in the Example 1147C and 1147D were used here to convert 1147B (50 mg) to the title lithium salt (30 mg, 45%, 2 steps). ^{1}HNMR (300 MHz, dmso-d_6) δ 7.44 (d, 1 H), 7.30 (m, 1 H), 7.25-7.08 (m, 4 H), 7.03 (m, 1 H), 6.87 (m, 1 H), 4.18 (m, 1 H), 3.66 (m, 1 H), 2.87 (t, 2 H), 2.60 (t, 2 H), 2.20-1.90 (m, 8 H), 1.75-1.00 (m, 22 H). MS(ESI–) m/z: 577 $(M-H)^-$.



Example 1150

N-[4-(N-adamant-1-ylaminocarbonylethyl)-2-(2-methylphenyl)benzoyl]methionine lithium salt

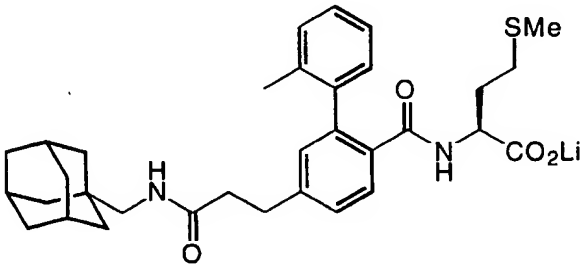
The procedures descriped in the Example 1147C and 1147D were used here to convert 1147B (50 mg) to the title lithium salt (40 mg, 62%, 2 steps). ^{1}HNMR (300 MHz, dmso-d_6) δ 7.63 (d, 1 H), 7.44 (d, 1 H), 7.27-7.05 (m, 5 H), 6.98 (m, 1 H), 6.88 (m, 1 H), 3.80 (m, 1 H), 3.64 (m, 1 H), 2.87 (m, 2 H), 2.50 (m, 2 H), 2.20-1.80 (m, 17 H), 1.77-1.45 (m, 8 H). MS(ESI–) m/z: 547 $(M-H)^-$.



Example 1151

N-[4-(N-adamant-2-ylaminocarbonylethyl)-2-(2-methylphenyl)benzoyl]methionine lithium salt

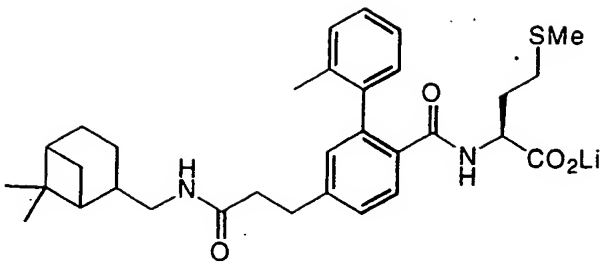
The procedures descriped in the Example 1147C and 1147D were used here to convert 1147B (50 mg) to the title lithium salt (41 mg, 64%, 2 steps). ^{1}HNMR (300 MHz, dmso-d_6) δ 7.44 (m, 1 H), 7.30-7.05 (m, 6 H), 7.00 (m, 1 H), 6.88 (m, 1 H), 3.67 (m, 1 H), 2.82 (m, 2 H), 2.35 (m, 2 H), 2.20 -1.45 (m, 25 H). MS(ESI–) m/z: 547 $(M-H)^-$.



Example 1154

N-[4-(N-adamant-1-ylmethylaminocarbonylethyl)-2-(2-methylphenyl)benzoyl]methionine lithium salt

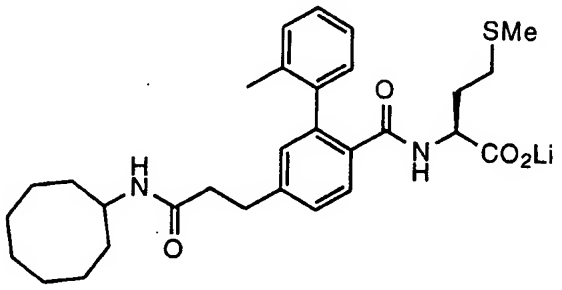
The procedures descriped in the Example 1147C and 1147D were used here to convert 1147B (50 mg) to the title lithium salt (47 mg, 72%, 2 steps). ^{1}HNMR (300 MHz, dmso-d_6) δ 7.61 (t, 1 H), 7.44 (d, 1 H), 7.25 (dd, 1 H), 7.24-7.08 (m, 4 H), 6.99 (br s, 1 H), 6.88 (m, 1 H), 3.62 (m, 1 H), 2.82 (t, 2 H), 2.73 (d, 2 H), 2.45 (t, 2 H), 2.20-1.90 (m, 8 H), 1.75-1.48 (m, 11 H), 1.35 (d, 6 H). MS(ESI–) m/z: 561 $(M-H)^-$.



Example 1155

N-[4-(N-Mytanylmethylaminocarbonylethyl)-2-(2-methylphenyl)benzoyl]methionine lithium salt

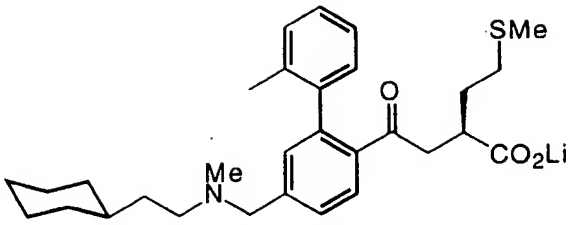
The procedures descriped in the Example 1147C and 1147D were used here to convert 1147B (50 mg) to the title lithium salt (45 mg, 70%, 2 steps). ^{1}H NMR (300 MHz, dmso-d_6) δ 7.60 (t, 1 H), 7.44 (d, 1 H), 7.28-7.08 (m, 5 H), 6.99 (br s, 1 H), 6.88 (m, 1 H), 3.66 (m, 1 H), 3.00 (m, 2 H), 2.83 (t, 2 H), 2.39 (t, 2 H), 2.33-1.20 (m, 19 H), 1.13 (s, 3 H), 0.97 (s, 3 H). MS(ESI–) m/z: 549 $(M-H)^-$.



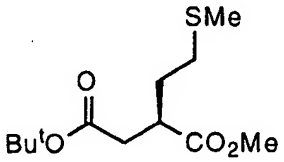
Example 1157

N-[4-(N-Cyclooctanylaminocarbonylethyl)-2-(2-methylphenyl)benzoyl]methionine lithium salt

The procedures descriped in the Example 1147C and 1147D were used here to convert 1147B (50 mg) to the title lithium salt (31 mg, 51%, 2 steps). ^{1}HNMR (300 MHz, dmso-d_6) δ 7.67 (d, 1 H), 7.44 (d, 1 H), 7.25-7.08 (m, 5 H), 6.96 (br s, 1 H), 6.88 (m, 1 H), 3.72 (m, 1 H), 3.63 (m, 1 H), 2.85 (t, 2 H), 2.36 (t, 2 H), 2.20-1.90 (m, 8 H), 1.90-1.30 (m, 16 H). MS(ESI–) m/z: 523 $(M-H)^-$.



13205 Example 1158

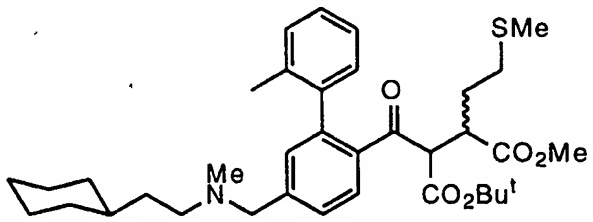


Example 1158A

Methyl 2-(tert-butoxycarbonylmethyl)-4-methylthiobutyrate

13210 To a -78 °C solution of methyl 4-methylthiobutyrate (1.48 g, 10.0 mmol) in THF (20 mL) was added sodium bis(trimethylsilyl)amide (1.0 M in THF, 11 mL). After 30 min, tert-butyl bromoacetate (2.34 g, 12.0 mmol) was added to the reaction, and the reaction mixture was gradually warmed to the room temperature over 6 hours. The reaction mixture was then partitioned between ethyl acetate (80 mL) and water (20 mL). The organic 13215 layer was washed with water (2 X 20 mL), brine (20 mL), dried over anhydrous magnesium sulfate, filtered and concentrated. The residue was purified by column chromatography with 5% ethyl acetate in hexane to give the title compound (1.21 g, 46%). ^{1}HNMR (300 MHz, $CDCl_3$) δ 3.75 (s, 3 H), 2.71 (t, 2 H), 2.51 (t, 2 H), 2.32 (m, 1 H), 2.06 (s, 1 H), 1.89 (t, 1 H), 1.41 (s, 9 H). MS(CI/NH_3) m/z: 263 $(M+H)^+$.

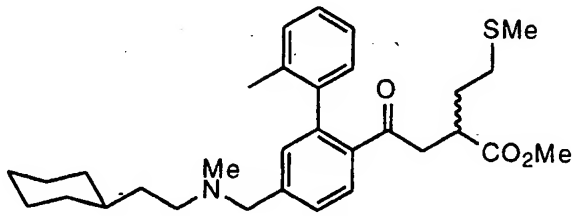
13220



Example 1158B

To a solution of the acid from example 608C (530 mg, 1.32 mmol) in DCM (2 mL) was added oxallyl chloride (2.0 M in DCM, 1.5 mL), followed by a small drop of DMF. 13225 After 2 hours at room temperature , the solvent was removed, and the residue was further dried under high vacuum (1 mmHg) for 1 hour. The solid (acid chloride) was redesolved in THF (5 mL).

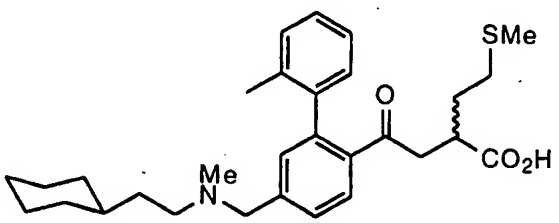
To a –78 °C solution of 1158A (1.21 g, 4.61 mmol) in THF (10 mL) in a separate flask was added sodium bis(trimethylsilyl)amide (1.0 M in THF, 5.28 mL). After 30 min., the acid chloride solution was added slowly to the reaction mixture via a cannula. After 1 hour, the reaction mixture was quenched with saturated aqueous ammonium chloride (3 mL) at – 78°C. After it reached the room temperature, the reaction mixture was then partitioned between ethyl acetate (80 mL) and water (20 mL). The organic layer was washed with sodium bicarbonate (saturated in water, 10 mL), water (2 X 10 mL), brine (20 mL), dried over anhydrous magnesium sulfate, filtered and concentrated. The residue was purified by column chromatography with 30% ethyl acetate in hexane to give the title compound (430 mg, 53%). ^{1}HNMR is messy because of 4 diastereomers exist. MS(CI/NH_3) m/z: 610 $(M+H)^+$.



Example 1158C

Methyl 3-[4-(N-cyclohexyl-N-methylaminomethyl)-2-(2-methylphenyl)benzoylmethyl]-4-methylthiobutyrate

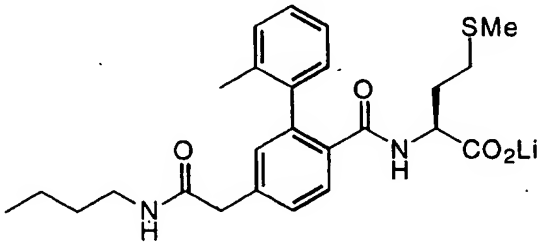
A solution of 1158B (420 mg, 0.69 mmol) in HCl (4.0 M in 1,4-dioxane, 5 mL) was heated at 80 °C for 2 hours. Solvent was evaporated, and the residue was redesolved in ethyl acetate (100 mL). The mixture was then washed with sodium bicarbonate (saturated in water, 20 mL), water (20 mL), brine (20 mL), dried over anhydrous magnesium sulfate, filtered and concentrated. The residue was purified by column chromatography with 30% ethyl acetate in hexane to give the title compound (121 mg, 34%). ^{1}HNMR (300 MHz, $CDCl_3$) δ 7.62 (d, 1 H), 7.40 (br d, 1 H), 7.31-7.12 (m, 4 H), 7.07 (br d, 1 H), 3.62 (s, 3 H), 3.54 (br s, 2 H), 2.85 (m, 1 H), 2.71 (m, 1 H), 2.40 (m, 2 H), 2.35-2.00 (m, 12 H), 1.80-0.80 (m, 15 H). MS(CI/NH_3) m/z: 510 $(M+H)^+$.



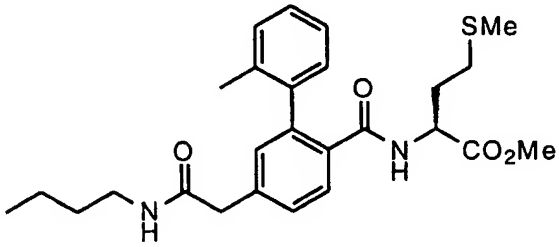
Example 1158D

3-[4-(N-Cyclohexyl-N-methylaminomethyl)-2-(2-methylphenyl)benzoylmethyl]-4-methylthiobutyric acid

The intermediate 1158C (112 mg) in MeOH (2 ML) and lithium hydroxide (1.0 M in water, 0.7 mL) was heated at 50 °C for 5 hours. The reaction mixture was then adjusted to pH 4-5 with KH_2PO_4 (saturated in water), and extracted with ethyl acetate (3 X 20 mL). The combined extracts were washed with brine, dried over anhydrous magnesium sulfate, filtered and concentrated to give the title compound (110 mg, 100%). ^{1}H NMR (300 MHz, dmso-d_6) δ 7.77 (m, 1 H), 7.61 (br d, 1 H), 7.40 (m, 1 H), 7.35-7.15 (m, 3 H), 7.07 (m, 1 H), 4.15 (br loop, 2 H), 2.88 (m, 2 H), 2.69 (m, 1 H), 2.28 (m, 2 H), 2.22-1.96 (m, 11 H), 1.72-0.80 (m, 15 H). MS(ESI–) m/z: 494 $(M-H)^-$.



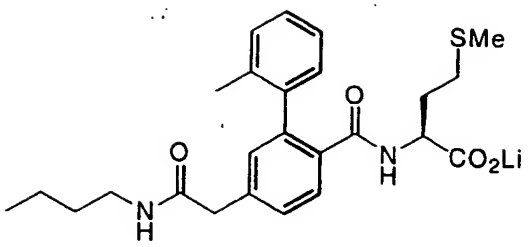
Example 1159



Example 1159A

N-[4-(N-butylaminocarbonylmethyl)-2-(2-methylphenyl)benzoyl]methionine lithium salt

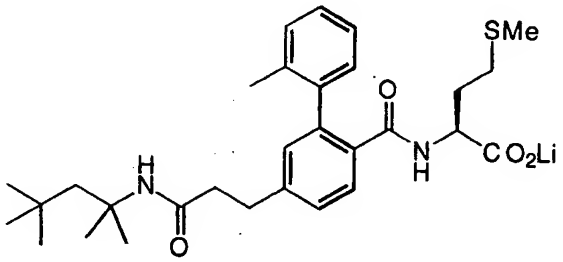
The procedures descriped in the Example 403E and 403F were used here to convert intermediate 1142A (61 mg, 0.18 mmol) to the title methyl ester (70 mg, 83%). ^{1}HNMR (300 MHz, $CDCl_3$) δ 7.95 (2 d's, 1 H), 7.39-7.15 (m, 5 H), 7.12 (br s, 1 H), 5.91 (br d, 1 H), 5.35 (m, 1 H), 4.63 (m, 1 H), 3.67 (s, 3 H), 3.61 (s, 2 H), 3.24 (q, 1 H), 2.20-1.99 (m, 8 H), 1.85 (m, 1 H), 1.60 (m, 1 H), 1.42 (m, 2 H), 1.27 (m, 2 H), 0.88 (t, 3 H). MS(CI/NH_3) m/z: 471 $(M+H)^+$.



Example 1159B

N-[4-(N-butylaminocarbonylmethyl)-2-(2-methylphenyl)benzoyl]methionine lithium salt

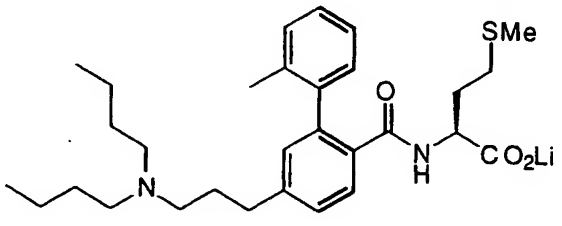
The procedure descriped in the Example 403I was used here to convert the intermediate 1159A (63 mg) to the title lithium salt (62 mg, 100%). ^{1}H NMR (300 MHz, dmso-d_6) δ 8.10 (t, 1 H), 7.57 (d, 1 H), 7.40 (br d, 1 H), 7.37-7.20 (m, 4 H), 7.17 (br s, 1 H), 7.04 (br d, 1 H), 3.75 (m, 1 H), 3.54 (s, 2 H), 3.13 (q, 2 H), 2.28-1.85 (m, 8 H), 1.78 (m, 1 H), 1.64 (m, 1 H), 1.47 (m, 2 H), 1.35 (m, 2 H), 0.93 (t, 3 H). MS(ESI–) m/z: 455 $(M-H)^-$.



Example 1160

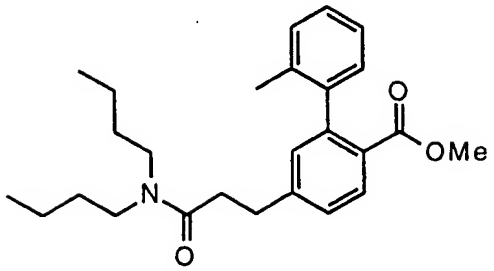
N-[4-(N-(2,2,4,4-tetramethylbutylamino)carbonylethyl)-2-(2-methylphenyl)benzoyl]methionine lithium salt

The procedures descriped in the Example 1147C and 1147D were used here to convert 1147B (50 mg) to the title lithium salt (50 mg, 81%, 2 steps). ^{1}HNMR (300 MHz, dmso-d_6) δ 7.44 (d, 1 H), 7.26 (br s, 1 H), 7.25-7.08 (m, 5 H), 6.98 (br s, 1 H), 6.88 (m, 1 H), 3.63 (m, 1 H), 2.82 (t, 2 H), 2.32 (t, 2 H), 2.20-1.90 (m, 8 H), 1.75-1.50 (m, 2 H), 1.67 (s, 2 H), 1.23 (s, 6 H), 0.89 (s, 9 H). MS(ESI–) m/z: 525 $(M-H)^-$.



Example 1161

13305



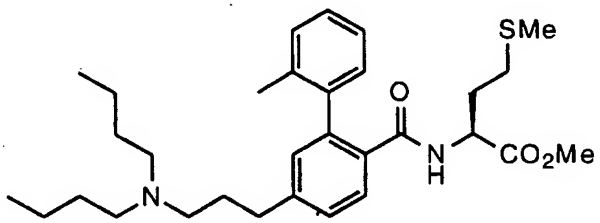
Example 1161A

Methyl 4-(N,N-Dibutylaminocarbonylethyl)-2-(2-methylphenyl)benzoyl

The procedure descriped in the Example 1144C was used here to convert the

13310 intermediate 1144B (150 mg, 0.5 mmol) and dibutylamine (129 mg, 1 mmol) to the title methyl ester (203 mg, 99%). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.90 (d, 1 H), 7.29-7.16 (m, 4 H), 7.06 (m, 2 H), 3.60 (s, 3 H), 3.30 (dt, 2 H), 3.14 (t, 2 H), 3.05 (t, 2 H), 2.61 (t, 2 H), 2.05 (s, 3 H), 1.46 (m, 2 H), 1.27 (m, 2 H), 0.90 (t, 6 H). MS(CI/NH_3) m/z: 410 $(M+H)^+$.

13315



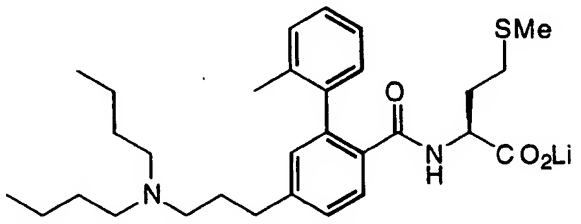
Example 1161B

N-[4-(N,N-Dibutylaminopropyl)-2-(2-methylphenyl)benzoyl]methionine Methyl Ester

The procedures descriped in the Example 403E and 403F were used here to convert

13320 the above intermediate 1161A (195 mg, 0.48 mmol) to the title methyl ester (165 mg, 66%). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.90 (2 d'd, 1 H), 7.35-7.19 (m, 5 H), 7.02 (br s, 1 H), 5.88 (br d, 1 H), 4.61 (m, 1 H), 3.65 (s, 3 H), 2.66 (t, 2 H), 2.40 (m, 6 H), 2.20-2.00 (m, 8 H), 1.90-1.70 (m, 3 H), 1.59 (m, 1 H), 1.45-1.20 (m, 8 H), 0.89 (t, 6 H). MS(CI/NH_3) m/z: 520 $(M+H)^+$.

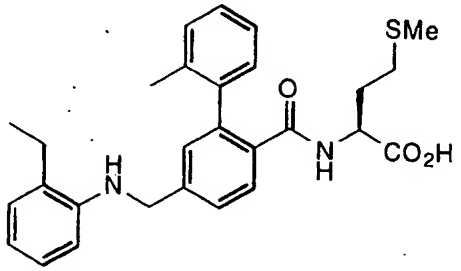
13325



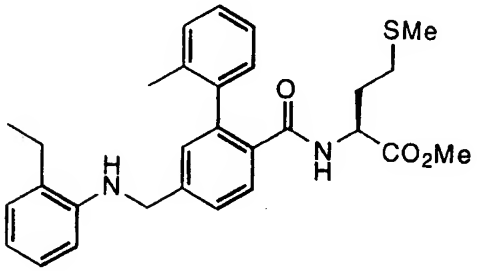
Example 1161C

N-[4-(N,N-Dibutylaminopropyl)-2-(2-methylphenyl)benzoyl]methionine lithium salt

The procedure descriped in the Example 403I was used here to convert the intermediate 1161B (156 mg) to the title lithium salt (151 mg, 98%). ^{1}H NMR (300 MHz, dmso-d_6) δ 7.46 (d, 1 H), 7.34-7.08 (m, 5 H), 6.97 (m, 2 H), 3.75 (m, 1 H), 2.63 (t, 2 H), 2.32 (m, 6 H), 2.20-1.80 (m, 9 H), 1.70 (m, 3 H), 1.60 (m, 1 H), 1.38-1.20 (m, 8 H), 0.84 (t, 6 H). MS(ESI–) m/z: 511 $(M-H)^-$.



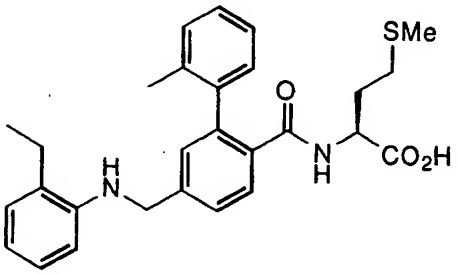
Example 1164



Example 1164A

N-[4-N-(2-Ethylphenyl)aminomethyl-2-(2-methylphenyl)benzoyl]methionine methyl ester

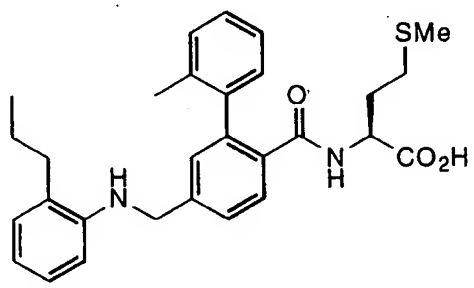
The desired ester was prepared using the method described inExample 403H starting with the compound described inExample 403G and 2-ethylaniline. m/e (ESI) 489 (MH^-)



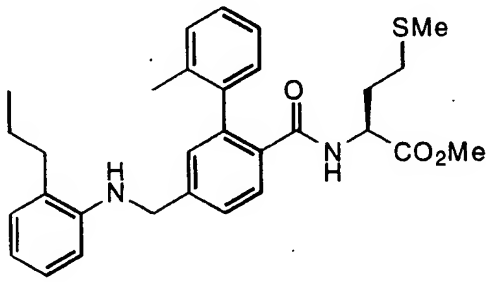
Example 1164B

N-[4-N-(2-Ethylphenyl)aminomethyl-2-(2-methylphenyl)benzoyl]methionine

The desired compound was prepared according to the method of Example 403I starting with compound prepared in Example 1164A. ^1H (300MHz, $CDCl_3$, δ) 7.96 (1H, t, J=9Hz), 7.48 (1H, bd, J=8Hz), 7.20-7.00 (8H, m), 6.77 (1H, t, J=9Hz), 6.57 (1H, bd, J=8Hz), 5.89 (1H, bd, J=8Hz), 4.58 (1H, m), 4.46 (2H, s), 2.55 (2H, q, J=8Hz), 2.20-2.00 (8H, m), 1.90 (1H, m), 1.57 (1H, m), 1.25 (3H, t, J=8Hz). m/e (ESI) 475 (MH^-) Anal.calc. for $C_{28}H_{32}N_2O_3S \cdot 0.25\ H_2O$ C 69.90, H 6.81, N 5.82 Found C 69.64, H 6.66, N 5.65



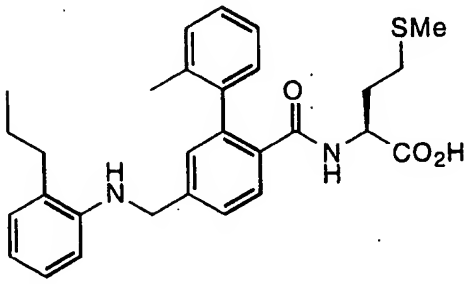
Example 1165



Example 1165A

N-[4-N-(2-Propylphenyl)aminomethyl-2-(2-methylphenyl)benzoyl]methionine methyl ester

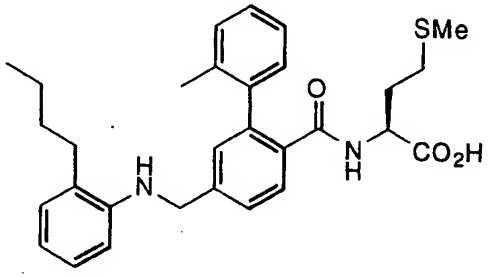
The desired ester was prepared using the method described in Example 403H starting with the compound described in Example 403G and 2-propylaniline. m/e (ESI) 503 (MH^-)



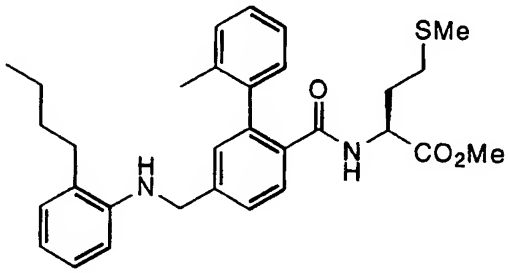
Example 1165B

N-[4-N-(2-Propylphenyl)aminomethyl-2-(2-methylphenyl)benzoyl]methionine

The desired compound was prepared according to the method ofExample 403I starting with compound prepared inExample 1165A. ^1H (300MHz, $CDCl_3$, δ) 7.98 (1H, t, J=9Hz), 7.47 (1H, dd, J=8&2Hz), 7.40-7.10 (6H, m), 7.03 (2H, m), 6.72 (1H, t, J=9Hz), 6.57 (1H, m), 5.86 (1H, bd, J=8Hz), 4.58 (1H, m), 4.44 (2H, s), 2.48 (2H, t, J=8Hz), 2.20-2.00 (8H, m), 1.91 (1H, m), 1.65 (2H, q, J=8Hz), 1.57 (1H, m), 1.01 (3H, t, J=8Hz). m/e (ESI) 489 (MH^-) Anal.calc. for $C_{29}H_{34}N_2O_3S \cdot 0.25\ H_2O$ C 70.34, H 7.02, N 5.66 Found C 70.33, H 6.88, N 5.44



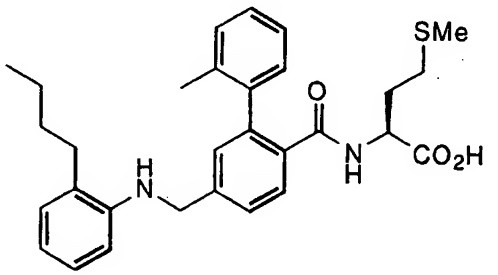
Example 1166



Example 1166A

N-[4-N-(2-Butylphenyl)aminomethyl-2-(2-methylphenyl)benzoyl]methionine methyl ester

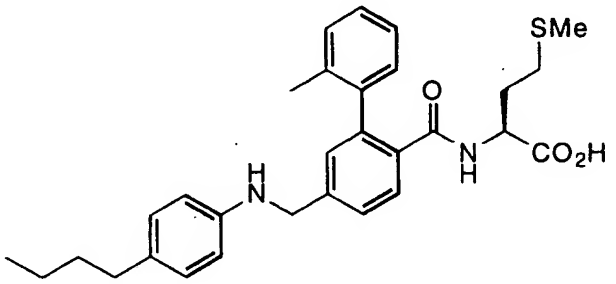
The desired ester was prepared using the method described inExample 403H starting with the compound described in Example 403G and 2-butylaniline. m/e (ESI) 517 (MH^-)



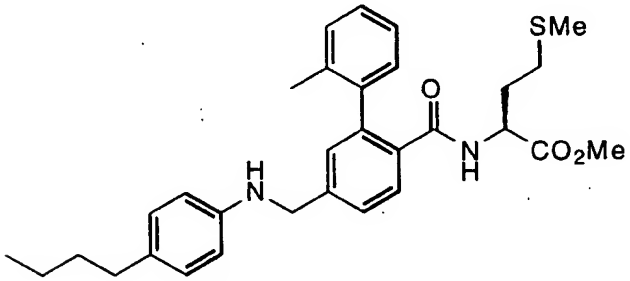
Example 1166B

N-[4-N-(2-Butylphenyl)aminomethyl-2-(2-methylphenyl)benzoyl]methionine

The desired compound was prepared according to the method ofExample 403I starting with compound prepared inExample 1166A. ^{1}H (300MHz, $CDCl_3$, δ) 7.97 (1H, t, J=9Hz), 7.45 (1H,bd, J=8), 7.40-7.10 (6H, m), 6.98 (2H, d, J=8Hz), 6.73 (1H, t, J=9Hz), 6.57 (1H, m), 5.87 (1H, bd, J=8Hz), 4.58 (1H, m), 4.45 (2H, s), 2.50 (2H, t, J=8Hz), 2.20-2.00 (8H, m), 1.91 (1H, m), 1.70-1.50 (3H, m), 1.40 (2H, q, J=8Hz), 0.93 (3H, t, J=8Hz). m/e (ESI) 503 (MH^-) Anal.calc. for $C_{30}H_{36}N_2O_3S \cdot 0.50\ H_2O$ C 70.14, H 7.26, N 5.45 Found C 70.39, H 7.08, N 5.24



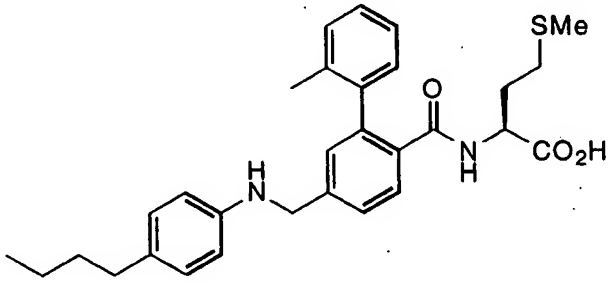
Example 1167



Example 1167A

N-[4-N-(4-Butylphenyl)aminomethyl-2-(2-methylphenyl)benzoyl]methionine methyl ester

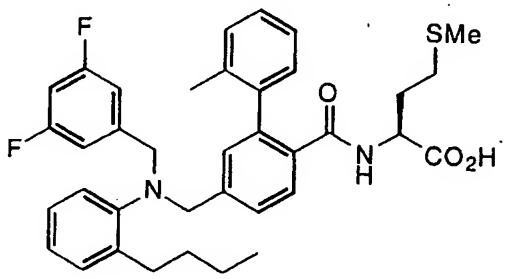
The desired ester was prepared using the method described inExample 403H starting with the compound described inExample 403G and 4-butylaniline. m/e (ESI) 517 (MH^-)



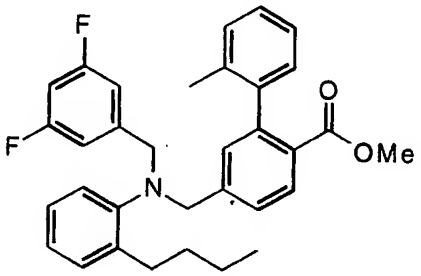
Example 1167B

N-[4-N-(4-Butylphenyl)aminomethyl-2-(2-methylphenyl)benzoyl]methionine

The desired compound was prepared according to the method of Example 403I starting with compound prepared inExample 1167A. ^{1}H (300MHz, $CDCl_3$, δ) 7.98 (1H, t, J=9Hz), 7.47 (1H,bd, J=8), 7.40-7.10 (6H, m), 7.04 (2H, d, J=9Hz), 6.56 (2H, d, J=9Hz), 5.88 (1H, bd, J=8Hz), 4.57 (1H, m), 4.40 (2H, s), 2.48 (2H, t, J=8Hz), 2.20-2.00 (8H, m), 1.90 (1H, m), 1.53 (3H, m), 1.32 (2H, m), 0.92 (3H, t, J=8Hz). m/e (ESI) 503 (MH^-) Anal.calc. for $C_{30}H_{36}N_2O_3S \cdot 0.25\ H_2O$ C 70.76, H 7.23, N 5.50 Found C 70.77, H 7.07, N 5.35



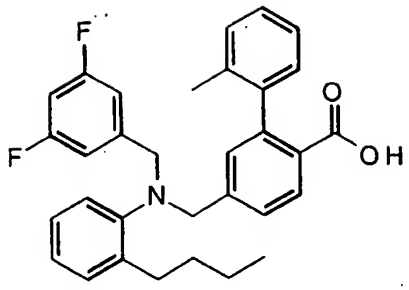
Example 1168



Example 1168A

4-N-(2-Butylphenyl)-N-(3,5-difluorobenzyl)aminomethyl-2-(2-methylphenyl)benzoic acid methyl ester

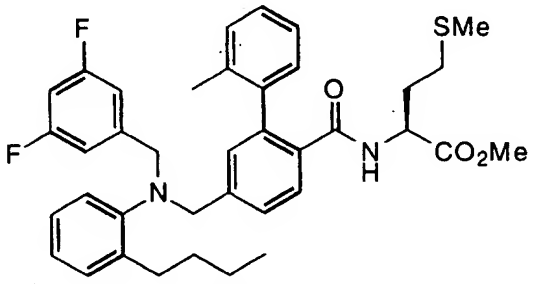
The desired compound was prepared using the method described inExample 1169A starting with 2-butylaniline, 3,5-difluorobenzylbromide, and 4-bromomethyl-2-(2-methylphenyl)benzoic acid methyl ester, prepared as inExample 1178A-D. m/e (ESI) 514 (MH^+)



Example 1168B

4-N-(2-Butylphenyl)-N-(3,5-difluorobenzyl)aminomethyl-2-(2-methylphenyl)benzoic acid

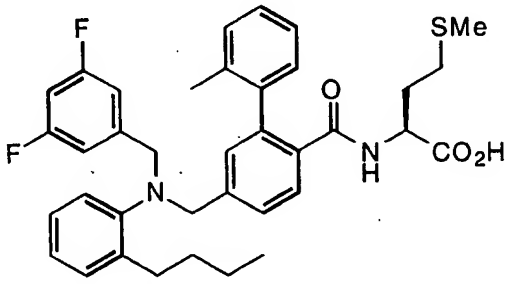
The desired acid was prepared using the method described in Example 403E starting with the product from Example 1168A.



Example 1168C

N-[4-N-(2-Butylphenyl)-N-(3,5-difluorobenzyl)aminomethyl-2-(2-methylphenyl)benzoyl]methionine methyl ester

The desired compound was prepared using the method described inExample 403F starting with the product fromExample 1168B. m/e (ESI) 645 (MH^+)



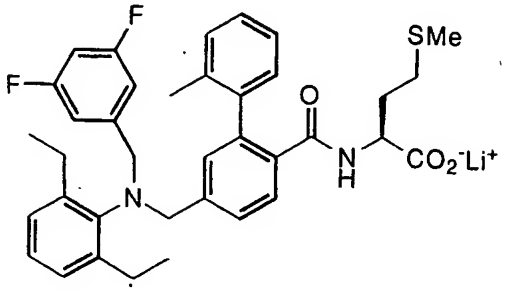
Example 1168D

N-[4-N-(2-Butylphenyl)-N-(3,5-difluorobenzyl)aminomethyl-2-(2-methylphenyl)benzoyl]methionine

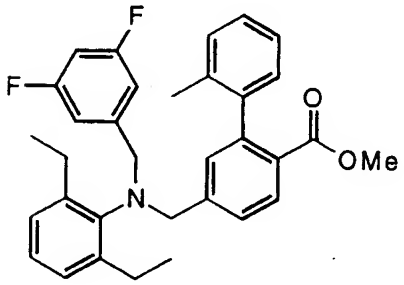
The desired compound was prepared according to the method ofExample 403I starting with the compound fromExample 1168C. ^1H (300MHz, $CDCl_3$, δ) 7.92 (1H, m), 7.40-6.90 (10H, m), 6.81 (2H, bd, J=8Hz), 6.66 (1H, m), 5.84 (1H, m), 4.55 (1H, m), 4.12 (2H, s), 4.04 (2H, s), 2.72 (2H, bt, J=9Hz), 2.20-1.80 (9H, m), 1.52 (3H, m), 1.36

(2H, m), 0.87 (3H, t, J=8Hz). m/e (ESI) 629 (MH^-) Anal.calc. for $C_{37}H_{40}F_2N_2O_3S$ C 70.45, H 6.39, N 4.40 Found C 70.10, H 6.27, N 4.35

13455



Example 1169



13460

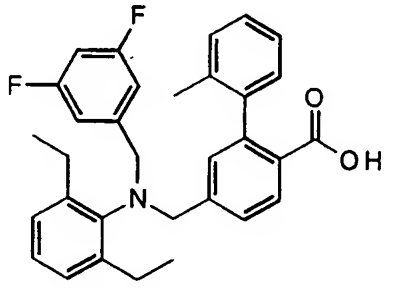
Example 1169A

4-N-(2,6-Diethylphenyl)-N-(3,5-difluorobenzyl)aminomethyl-2-(2-methylphenyl)benzoic acid methyl ester

4-Bromomethyl-2-(2-methylphenyl)benzoic acid methyl ester (100 mg, 0.31 mmol), prepared as inExample 1178A-D, 2,6-diethylaniline (0.062 mL, 0.38 mmol), and

13465 diisopropylethylamine (0.084 mL, 0.470 mmol) were dissolved in DMF (5 mL), and solution stirred overnight at room temperature. To this mixture was then added diisopropylethylamine (0.084 mL, 0.470 mmol) and α-bromo-3,5-difluorotoluene (0.100 mL, 0.760 mmol), and reaction heated at 80°C for 3 days. Solvents concentrated in vacuo, and residue purified by flash chromatography on silica gel eluting with 2% EtOAc/Hexanes

13470 to afford the desired compound as a yellow oil (72 mg, 45%). m/e (ESI) 514 (MH^+)

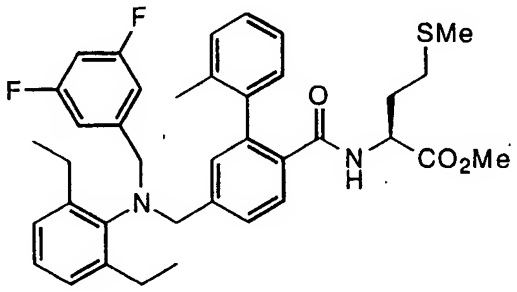


Example 1169B

4-N-(2,6-Diethylphenyl)-N-(3,5-difluorobenzyl)aminomethyl-2-(2-methylphenyl)benzoic acid

13475

The desired acid was prepared using the method described in Example 403E starting with the product from Example 1169A.



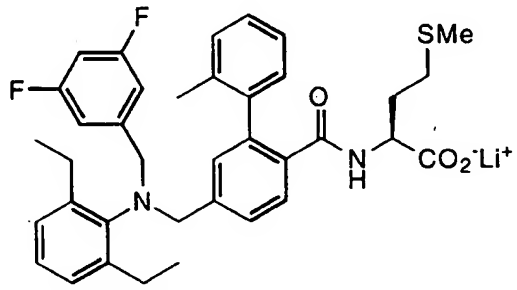
13480

Example 1169C

N-[4-N-(2,6-Diethylphenyl)-N-(3,5-difluorobenzyl)aminomethyl-2-(2-methylphenyl)benzoyl]methionine methyl ester

The desired compound was prepared using the method described inExample 403F starting with the product fromExample 1169B. m/e (ESI) 645 (MH^+)

13485



Example 1169D

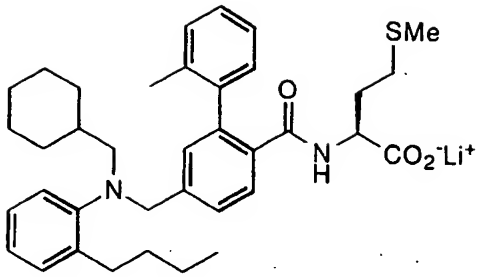
N-[4-N-(2,6-Diethylphenyl)-N-(3,5-difluorobenzyl)aminomethyl-2-(2-methylphenyl)benzoyl]methionine lithium salt

13490

The desired compound was prepared according to the method ofExample 403I starting with the compound fromExample 1169C. ^1H (300MHz, DMSO, δ) 7.43 (1H, d, J=9Hz), 7.30-7.00 (9H, m), 6.85 (4H, m), 4.21 (2H, s), 4.18 (2H, s), 3.65 (1H, m), 2.60-2.40 (4H, m), 2.10-1.50 (10H, m), 1.03 (6H, t, J=8Hz). m/e (ESI) 629 (MH^-) Anal.calc. for $C_{37}H_{39}F_2LiN_2O_3S \cdot 1.50\ H_2O$ C 66.95, H 6.38, N 4.22 Found C 66.79, H

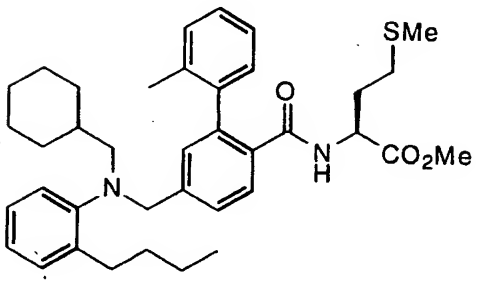
13495

6.34, N 3.93



Example 1170

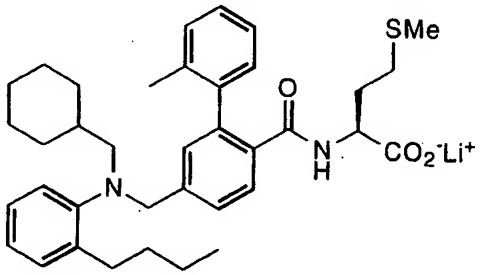
13500



Example 1170A

N-[4-N-(2-Butylphenyl)-N-(cyclohexylmethyl)aminomethyl-2-(2-methylphenyl)benzoyl]methionine methyl ester

13505 The desired ester was prepared using the method described in Example 403H starting with the compound described in Example 1166A and cyclohexanecarboxaldehyde. m/e (ESI) 613 (MH^-)



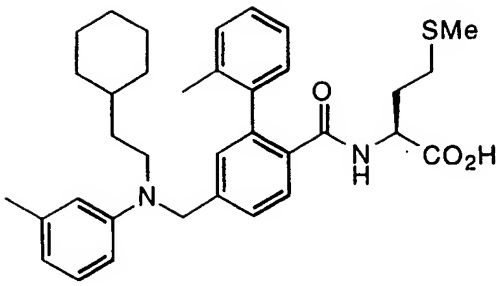
13510

Example 1170B

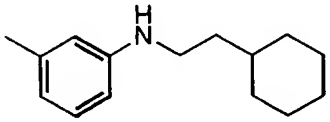
N-[4-N-(2-Butylphenyl)-N-(cyclohexylmethyl)aminomethyl-2-(2-methylphenyl)benzoyl]methionine lithium salt

The desired compound was prepared according to the method of Example 403I starting with compound prepared in Example 1170A. ^1H (300MHz, DMSO, δ) 7.47 (1H, d,

13515 J=9Hz), 7.29 (1H, m), 7.25-6.95 (9H, m), 6.90 (1H, m), 3.97 (2H, s), 3.16 (1H, m), 2.70 (4H, m), 2.10-1.85 (7H, m), 1.70 (3H, m), 1.60-1.40 (6H, m), 1.40-1.15 (4H, m), 1.05 (3H, m), 0.79 (5H, t, J=8Hz). m/e (ESI) 599 (MH^-) Anal.calc. for $C_{37}H_{47}LiN_2O_3S \cdot 1.00\ H_2O$ C 71.13, H 7.90, N 4.48 Found C 71.01, H 7.93, N 4.14



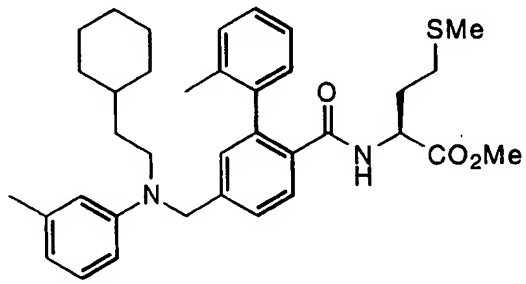
Example 1171



Example 1171A

N-(2-Cyclohexylethyl)-N-(3-methylphenyl)amine

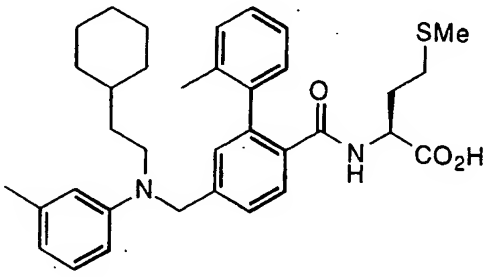
To a stirred solution at ambient temperature of cyclohexylacetic acid (500 mg, 3.52 mmol) and 3-methylaniline (0.45 mL, 4.22 mmol) in DMF (10 mL) was added 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide (809 mg, 4.22 mmol). Reaction stirred overnight at ambient tenperature. Reaction diluted with EtOAc and washed with water, 1.0M $NaHCO_3$ (2x), 1N H_3PO_4 (2x), and brine. Organic layer dried with Na_2SO_4, filtered, and concentrated in vacuo. To a solution at ambient temperature under N_2 of this residue in anhydrous THF (3 mL) was added a 1.0M lithium aluminum hydride solution (7.00 mL, 7 mmol) in THF. Reaction refluxed overnight. Reaction cooled to 0°C and quenched with successive addition of water (0.27 mL), 15% aqueous NaOH (0.27 mL), and water (0.80 mL). Mixture stirred 30 minutes at ambient temperature, and solids filtered off through celite and washed with EtOAc. Filtrate dried with Na_2SO_4, filtered, and concentrated in vacuo to produce a colorless oil. m/e (DCI/NH_3) 218 (MH^+)



Example 1171B

N-[4-N-(2-Cyclohexylethyl)-N-(3-methylphenyl)aminomethyl-2-(2-methylphenyl)benzoyl]methionine methyl ester

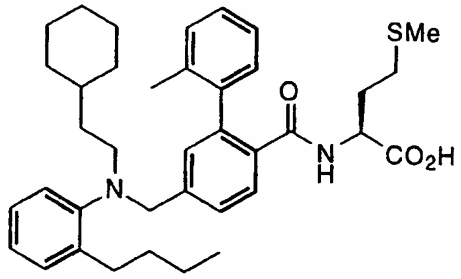
The desired ester was prepared using the method described in Example 403H starting with the compounds described in Example 403G and Example 1171A. m/e (ESI) 585 (MH^-)



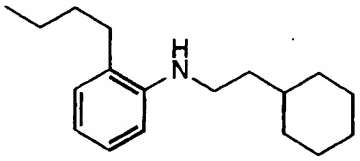
Example 1171C

N-[4-N-(2-Cyclohexylethyl)-N-(3-methylphenyl)aminomethyl-2-(2-methylphenyl)benzoyl]methionine

The desired compound was prepared according to the method of Example 403I starting with compound prepared in Example 1171B. ^1H (300MHz, $CDCl_3$, δ) 7.92 (1H, t, J=9Hz), 7.40-7.00 (8H, m), 6.47 (2H, m), 5.86 (1H, d, J=8Hz), 4.51 (4H, m), 3.39 (2H, m), 2.25 (3H, s), 2.15-1.80 (8H, m), 1.70 (5H, m), 1.50 (3H, m), 1.40-1.05 (4H, m), 0.96 (2H, m). m/e (ESI) 571 (MH^-) Anal.calc. for $C_{35}H_{44}N_2O_3S \cdot 1.00\ H_2O$ C 71.15, H 7.85, N 4.74 Found C 70.91, H 7.89, N 4.46



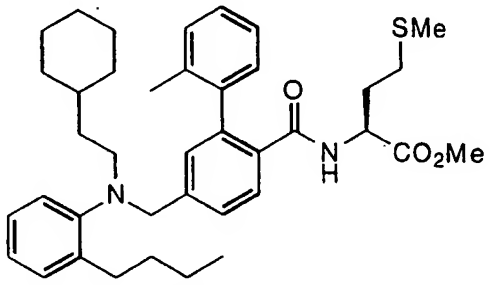
Example 1172



Example 1172A

N-(2-Butylphenyl)-N-(2-cyclohexylethyl)amine

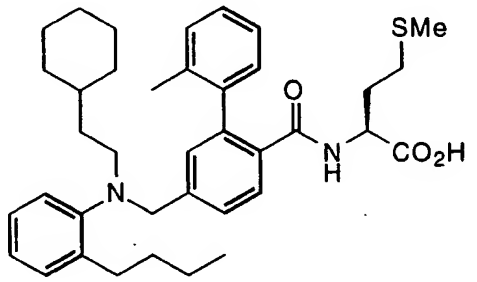
The desired amine was prepared using the method described in Example 1171A starting with cyclohexylacetic acid and 2-butylaniline. m/e (DCI/NH_3) 260 (MH^+)



Example 1172B

N-[4-N-(2-Butylphenyl)-N-(2-cyclohexylethyl)aminomethyl-2-(2-methylphenyl)benzoyl]methionine methyl ester

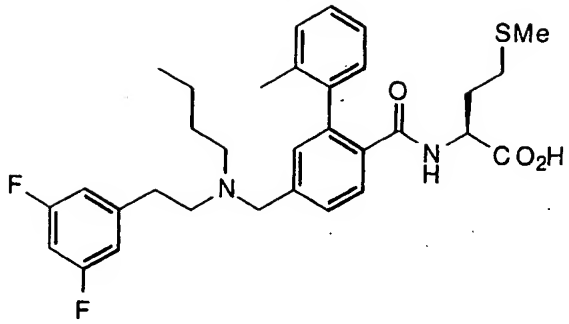
The desired ester was prepared using the method described in Example 403H starting with the compounds described in Example 403G and Example 1172A. m/e (ESI) 627 (MH^-)



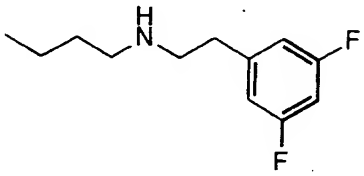
Example 1172C

N-[4-N-(2-Butylphenyl)-N-(2-cyclohexylethyl)aminomethyl-2-(2-methylphenyl)benzoyl]methionine

The desired compound was prepared according to the method of Example 403I starting with compound prepared in Example 1172B. ^1H (300MHz, $CDCl_3$, δ) 7.94 (1H, t, J=9Hz), 7.41 (1H, bd, J=8HZ), 7.40-7.00 (9H, m), 5.85 (1H, dd, J=8&2Hz), 4.55 (1H, m), 4.07 (2H, s), 2.91 (2H, m), 2.68 (2H, m), 2.20-1.80 (9H, m), 1.70-1.40 (8H, m), 1.40-1.00 (8H, m), 0.86 (3H, t, J=8Hz), 0.79 (2H, m). m/e (ESI) 613 (MH^-) Anal.calc. for $C_{38}H_{50}N_2O_3S \cdot 0.25\ H_2O$ C 73.69, H 8.22, N 4.52 Found C 73.74, H 8.17, N 4.30



Example 1173



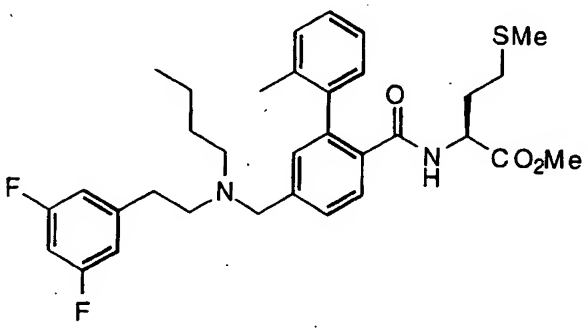
13590

Example 1173A

N-(2-Butylphenyl)-N-(2-(3,5-difluoro)phenylethyl)amine

The desired amine was prepared using the method described in Example 1171A starting with 3,5-difluorophenylacetic acid and butylamine. m/e (DCI/NH_3) 214 (MH^+)

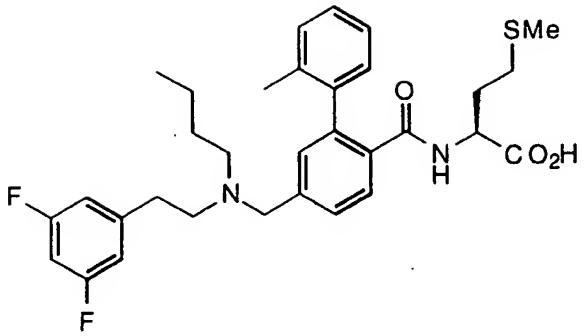
13595



Example 1173B

N-[4-N-Butyl-N-(2-(3,5-difluoro)phenylethyl)aminomethyl-2-(2-methylphenyl)benzoyl]methionine methyl ester

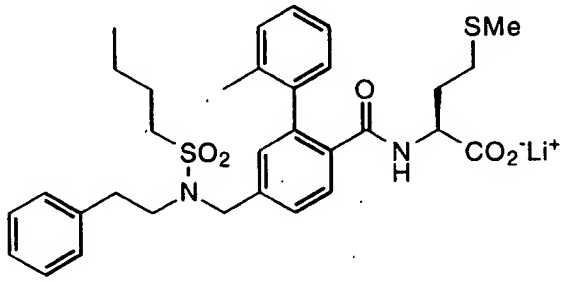
13600 The desired ester was prepared using the method described in Example 403H starting with the compounds described in Example 403G and Example 1173A. m/e (ESI) 581 (MH^-)



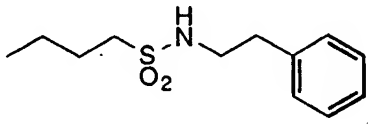
Example 1173C

N-[4-N-Butyl-N-(2-(3,5-difluoro)phenylethyl)aminomethyl-2-(2-methylphenyl)benzoyl]methionine

The desired compound was prepared according to the method ofExample 403I starting with compound prepared inExample 1173B. ^{1}H (300MHz, $CDCl_3$, δ) 7.80 (1H, d, J=9Hz), 7.54 (1H, m), 7.40-7.00 (5H, m), 6.80-6.60 (3H, m), 6.17 (1H, m), 4.43 (1H, m), 4.00 (2H, m), 2.98 (4H, m), 2.81 (2H, m), 2.20-1.80 (9H, m), 2.60 (3H, m), 1.30 (2H, m), 0.92 (3H, t, J=8Hz). m/e (ESI) 567 (MH^-) Anal.calc. for $C_{32}H_{38}F_2N_2O_3S \cdot 0.50\ H_2O$ C 66.53, H 6.80, N 4.85 Found C 66.67, H 6.67, N 4.69



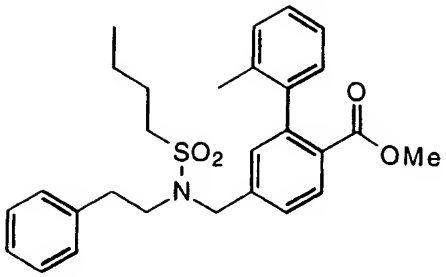
Example 1174



Example 1174A

N-(Butanesulfonyl)-N-(2-phenylethyl)amine

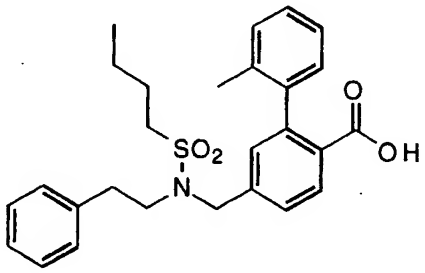
To a stirred solution at ambient temperature of phenethylamine (200 mg, 1.65 mmol) in CH_2Cl_2 (2 mL) was added triethylamine (0.35 mL, 2.48 mmol) and butanesulfonyl chloride (0.24 mL, 1.82 mmol). After 4 hours of stirring at ambient temperature, the reaction was diluted with EtOAc and washed with water, 1.0M $NaHCO_3$, and brine. Organic layer dried with Na_2SO_4, filtered, and concentrated in vacuo.



Example 1174B

4-(N-Butanesulfonyl-N-(2-phenylethyl)aminomethyl)-2-(2-methylphenyl)benzoic acid methyl ester

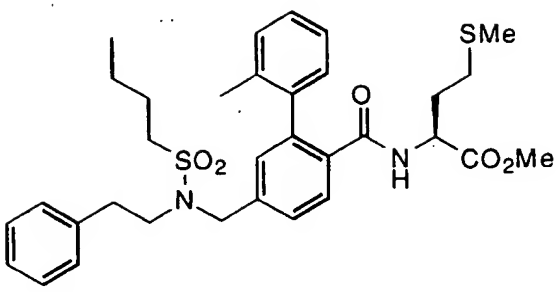
To a stirred mixture in anhyrous DMF (1 mL) at room temperature under N_2 of 60% sodium hydride suspension in mineral oil (30 mg, 0.752) was added N-(butanesulfonyl)-N-(2-phenylethyl)amine (181 mg, 0.752 mmol), prepared as inExample 1174A. Reaction stirred 20 minutes, and then, a solution of 4-bromomethyl-2-(2-methylphenyl)benzoic acid methyl ester (200 mg, 0.627 mmol), prepared as inExample 1178A-D, in anhydrous DMF (5 mL) was added. Reaction stirred overnight at room temperature. Reaction quenched with 1N H_3PO_4 and diluted with EtOAc. Organic layer separated, washed with brine, dried with $Na2SO_4$, filtered, and concentrated in vacuo. Residue purified by flash chromatography on silica gel (15% EtOAc/Hexanes) to afford the desired product as a pale yellow oil (293 mg, 98%). m/e (ESI) 480 (MH^+)



Example 1174C

4-(N-Butanesulfonyl-N-(2-phenylethyl)aminomethyl)-2-(2-methylphenyl)benzoic acid

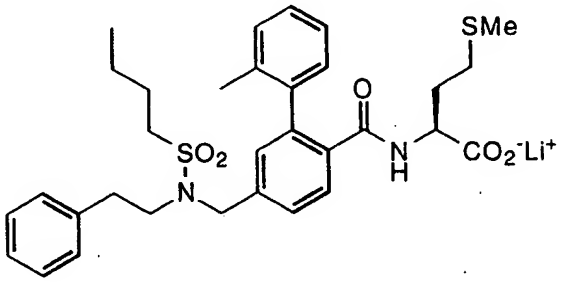
The desired acid was prepared using the method described in Example 403E starting with the product from Example 1174B.



Example 1174D

N-[4-N-Butanesulfonyl-N-(2-phenylethyl)aminomethyl-2-(2-methylphenyl)benzoyl]methionine methyl ester

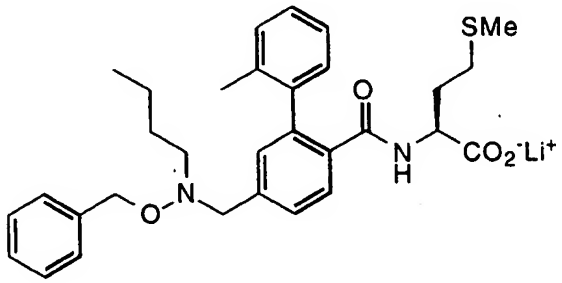
The desired compound was prepared using the method described in Example 403F starting with the product from Example 1174C. m/e (ESI) 480 (MH^-)



Example 1174E

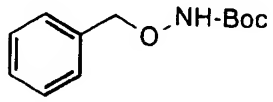
N-[4-N-Butanesulfonyl-N-(2-phenylethyl)aminomethyl-2-(2-methylphenyl)benzoyl]methionine lithium salt

The desired compound was prepared according to the method of Example 403I starting with compound prepared in Example 1174D. ^1H (300MHz, DMSO-d6, δ) 7.62 (1H, d, J=7Hz), 7.52 (1H, dd, J=7&2Hz), 7.20-7.10 (10H, m), 7.14 (1H, bd, J=7Hz), 4.65 (2H, bs), 3.76 (1H, m), 3.00 (2H, m), 2.78 (2H, m), 2.25-2.00 (5H, m), 1.99 (3H, s), 1.90-1.70 (4H, m), 1.62 (2H, m), 1.37 (2H, m), 0.92 (3H, t, J=8Hz). m/e (ESI) 595 (MH^-) Anal.calc. for $C_{32}H_{39}LiN_2O_5S_2 \cdot 0.50\ H_2O$ C 62.83, H 6.59, N 4.38 Found C 62.59, H 6.59, N 4.44



Example 1175

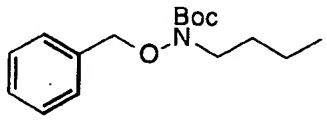
13670 *N*-[4-*N*--Benzyloxy-*N*-butylaminomethyl-2-(2-methylphenyl)benzoyl]methionine lithium salt



Example 1175A

13675 *N*--t-Butoxycarbonyl-*O*-benzylhydroxylamine

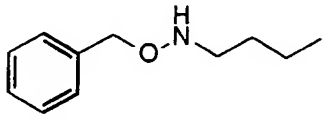
To a stirred solution at 0°C of *O*-benzylhydroxylamine hydrochloride in THF was added diisopropylethylamine (2.5 equiv.) and di-t-butyldicarbonate (1.2 equiv.). Reaction stirred one hour at 0°C and overnight at ambient temperature. Reaction concentrated *in vacuo*. Residue taken up in EtOAc and washed with water, 1.0M $NaHCO_3$, 1N H_3PO_4, 13680 and brine. Organic layer dried with Na_2SO_4, filtered, and evaporated.



Example 1175B

N--t-Butoxycarbonyl-*N*-butyl-*O*-benzylhydroxylamine

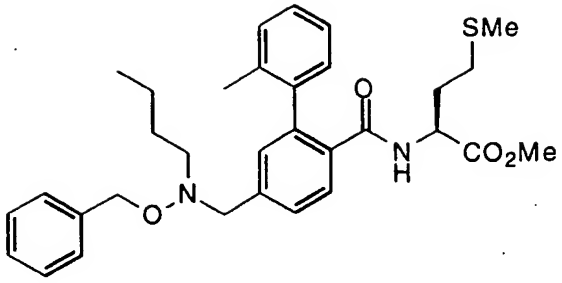
13685 To a stirred solution at 0°C of *N*--t-Butoxycarbonyl-*O*-benzylhydroxylamine, prepared as in Example 1175A, in anhydrous THF was added portionwise a 60% dispersion of sodium hydride (1.2 equiv.) in mineral oil. Mixture stirred 30 minutes ar 0°C, and then, 1-iodobutane (1.2 equiv.) was added dropwise. Reaction stirred one hour at 0°C, and than, overnight at room temperature. Reaction concentrated *in vacuo*. Residue taken up 13690 in EtOAc and washed with water, 1.0M $NaHCO_3$, 1N H_3PO_4, and brine. Organic layer dried with Na_2SO_4, filtered, and evaporated.



Example 1175C

13695 *N*-Butyl-*O*-benzylhydroxylamine hydrochloride salt

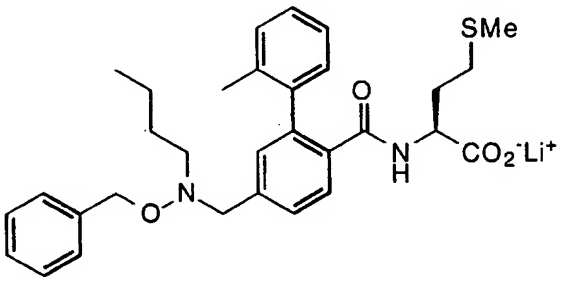
The desired compound was prepared using the method described in Example 403D starting with the compound prepared in Example 1175B.



Example 1175D

N-[4-*N*--Benzyloxy-*N*-butylaminomethyl-2-(2-methylphenyl)benzoyl]methionine methyl ester

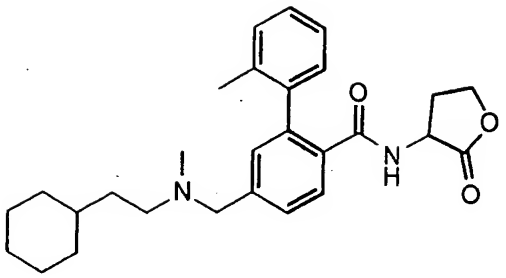
The desired ester was prepared using the method described in Example 403H starting with the compound prepared in Example 1175C and *N*-[4-Formyl-2-(2-methylphenyl)benzoyl]methionine methyl ester, prepared as in Example 403G. m/e (ESI) 547 (MH^-)



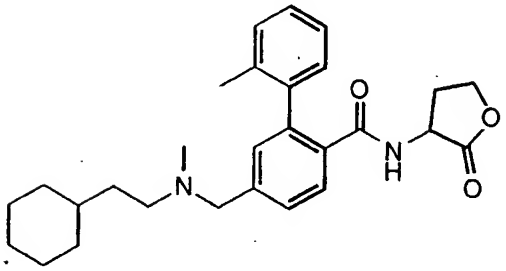
Example 1175E

N-[4-*N*--Benzyloxy-*N*-butylaminomethyl-2-(2-methylphenyl)benzoyl]methionine lithium salt

The desired compound was prepared according to the method of Example 403I starting with the compound in Example 1175D. ^1H (300MHz, DMSO-d6, δ) 7.52 (1H, d, J=9Hz), 7.40 (1H, dd, J=7&2Hz), 7.30-7.10 (10H, m), 6.96 (1H, bd, J=7Hz), 4.46 (2H, bs), 3.87 (2H, bs), 3.71 (1H, m), 2.68 (2H, t, J=8Hz), 2.25-1.95 (5H, m), 1.93 (3H, s), 1.90-1.60 (2H, m), 1.50 (2H, m), 1.30 (2H, m), 0.83 (3H, t, J=8Hz). m/e (ESI) 533 (MH^-) Anal.calc. for $C_{31}H_{37}LiN_2O_4S \cdot 0.75\ H_2O$ C 67.19, H 7.00, N 5.05 Found C 67.19, H 6.91, N 4.96



Example 1177

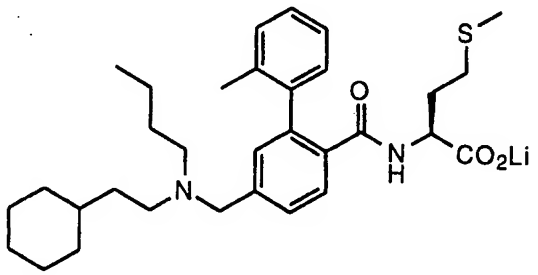


13725

Example 1177

N-[4-N-(2-Cyclohexylethyl)-N-methylaminomethyl-2-(2-methylphenyl)benzoyl]3-aminotetrahydrofuran-2-one

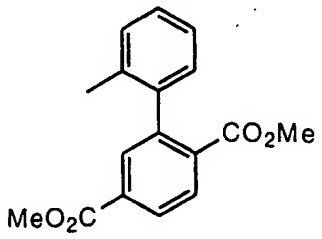
The desired compound was prepared using the method of Example 403F starting with 4-(N-(2-cyclohexylethyl)-N-methylaminomethyl)-2-(2-methylphenyl)benzoic acid,
13730 prepared as in Example 608C, and α-amino-γ-butyrolactone hydrobromide.
^{1}H (300MHz, $CDCl_3$, δ) (rotamer) 7.91 (1H, t, J=9Hz), 7.41 (1H, bd, J=8HZ), 7.35-7.20 (4H, m), 7.19 (1H, d, J=2Hz), 5.72 (1H, m), 4.49 (1H, m), 4.33 (1H, bt, J=8Hz), 4.17 (1H, m), 3.53 (2H, s), 2.62 (1H, m), 2.39 (2H, t, J=8Hz), 2.20 (3H, s), 2.15 (2.07) (3H, s), 1.80-1.50 (7H, m), 1.38 (2H, m), 1.30-1.10 (3H, m), 0.89 (2H, m). m/e (ESI)
13735 447 (MH^-) Anal.calc. for $C_{28}H_{36}N_2O_3 \cdot 1.00\ H_2O$ C 72.07, H 8.21, N 6.00 Found C 72.12, H 8.03, N 5.76



13740

Example 1178

N-[4-(*N*-(-2-cyclohexylethyl)-*N*-butylaminomethyl)-2-(2-methylphenyl)benzoyl]methionine, Lithium Salt

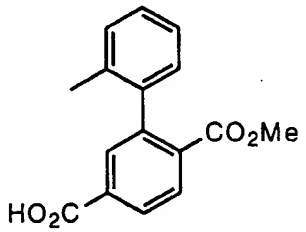


13745

Example 1178A

Dimethyl-(2-methylphenyl)terephthalate

A mixture of dimethyliodoterephthalate (278 g, 0.87 mol), 2-methylphenylboronic acid (141 g, 1.04 mol) palladium (II) acetate (1.95 g, 0.0087 mol) and triphenylphosphine (9.1 g, 0.035 mol) in 2.2 L of toluene and 2.2 L of 2M sodium carbonate was degassed with nitrogen and heated to 80°C for 1.5 hours and cooled to ambient temperature. The layers were separated and the organic layer filtered through a plug of silica gel (600g) prewetted with methyl t-butylether (MTBE, 1.2 L). The frit was washed with 5 L of MTBE. The mixture was then concentrated to provide 237 g (96%) of the title compound. ^{1}H NMR ($CDCl_3$) δ 8.09, dd, 1H; 8.02, d, 1H; 7.95, d, 1H; 7.20 - 7.34, m, 3H; 7.10, bd, 1H; 3.96, s, 3H; 3.64, s, 3H; 2.08, s, 3H. MS (DCI/NH_3) 302 $(M + NH_4)^+$.

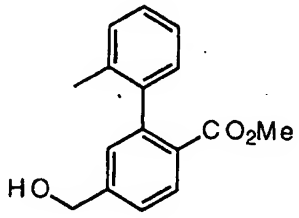


Example 1178B

2-(2-methylphenyl)-4-carboxybenzoic acid, methyl ester

A solution of example 1178A (194 g, 0.68 mol) in 2:1 THF/methanol (~0.3M) was cooled to 0°C and lithium hydroxide (0.38 L of a 2.2 M aqueous solution, 0.82 mol) was added such that the reaction temperature remained below 10°C. The cooling bath was removed and the mixture allowed to warm to 11°C overnight and then warmed to ~ 20°C over 4 hours. The mixture was concentrated to a volume of ~ 1.2 L and then diluted to 5.6 L with water. The mixture was extracted with hexanes and the aqueous layer filtered through celite (~200 g) and the celite pad washed with water. The mixture was diluted with ethyl acetate (6 L) and the pH of the aqueous phase adjusted to 5.5 by the addition of 3M aqueous HCl (~ 250 mL). The organic phase was removed and concentrated to provide 171 g (93%) of the

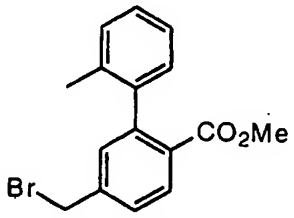
title compound. The material was ~ 87% pure. An analytical sample was obtained by recrystallization from aqueous ethanol. ^{1}H NMR ($CDCl_3$) δ 8.14, dd, 1H; 8.03, d, 1H; 8.01, d, 1H; 7.28 - 7.42, m, 3H; 7.09, bd, 1H; 3.64, s, 3H; 2.08, s, 3H. MS (DCI/NH_3): 271 $(MH)^+$; 288 $(M + NH_4)^+$.



Example 1178C

4-hydroxymethyl-2-(2-methylphenyl)benzoic, methyl ester

A solution of example 1178B (4.67g, 17.3 mmol) in 35 mL of THF was cooled in an ice bath and treated with borane (0.88M in THF, 39 mL, 34.6 mmol) such that the internal temperature remained below 10°C. The cooling bath was removed and the solution stirred for 3 hours and then cooled in an ice bath. The reaction was quenched by the careful addition of 8 mL of water (vigorous evolution of hydrogen gas) keeping the temperature below 10°C. An additional 8 mL of water was added and the mixture partitioned between ethyl acetate and 2N sodium hydroxide. The layers were separated and the organic layer was extracted with water, dried, filtered and concentrated. The residue was purified by column chromatography on silica gel to provide 3.90 g (88%) of the title compound. ^{1}H NMR ($CDCl_3$) δ 7.98, d, 1H; 743, dd, 1H; 7.16 - 7.28, m, 4H; 7.07, bd, 1H; 4.77, s, 2H; 3.62, s, 3H; 2.05, s, 3H; 1.78, bs, 1H. MS (DCI/NH_3): 257 $(MH)^+$; 274 $(M + NH_4)^+$.

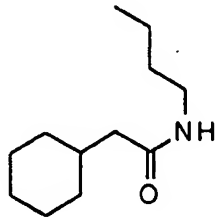


Example 1178D

4-bromomethyl-2-(2-methylphenyl)benzoic, methyl ester

A solution of 36 g (140 mmol) of example 1178C and 13.4 g (154 mmol) lithium bromide in DMF (150 mL) was chilled in an ice-water bath, then 40.3 g (14.0 mL, 149 mmol) phosphorous tribromide was added, followed by more DMF (50 mL). After 15 minutes the reaction was partitioned between water (1200 mL) and Et_2O (600 mL). The aqueous layer was extracted with Et_2O (2 x 150 mL), then the combined Et_2O layers were

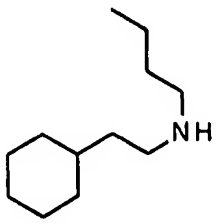
washed with brine, and dried over Na_2SO_4. After filtration and concentration, recovered 44.5 g (97.5%) slightly cloudy, almost colorless oil that was 2% DMF by weight (determined by NMR). ^1H NMR ($CDCl_3$) δ 7.84 (d, 1H), 7.44 (dd, 1H), 7.24 (m, 4H), 7.07 (br d, 1H), 4.50 (s, 2H), 3.62 (s, 3H), 2.07 (s, 3H). MS (DCI/NH3) 336/338 $(M+H+NH_3)^+$.



Example 1178E

N-butyl-N-2-cyclohexylacetamide

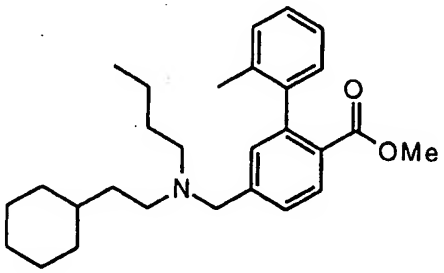
2-Cyclohexylacetic acid (42.66 g, 0.30 mol) was dissolved in 85 mL of thionyl chloride and the mixture heated to reflux for 2 hours. After cooling to room temperature, the yellow solution was concentrated. Toluene was added and the solution was concentrated again and the acid chloride used directly. The acid chloride was diluted with 100 mL of methylene chloride and this solution added to a biphasic mixture of butylamine (60 mL, 0.60 mol) in 100 mL of methylene chloride and 2M aqueous potassium carbonate (150 mL) and the mixture was stirred overnight at ambient temperature. An additional 30 mL of butylamine was added and stirring continued for 2 hours and then the mixture was poured into a separatory funnel. The layers were separated and the aqueous phase was extracted with 1 portion of methylene chloride and the combined organic extracts were dried, filtered and concentrated to an off white solid. This material was suspended in 400 mL of 1:1 ether/hexanes and filtered. The solid was washed with 2 additional portions of 1:1 ether/hexanes. The filtrates were extracted with 3 portions of aqueous HCl, dried, filtered and concentrated to a volume of ~ 200 mL. The solid that formed was collecterd by filtration and combined with the previous solid material and dried under vacuum to give the title compound (49.50 g, 88%). ^1H nmr (300 MHz., $CDCl_3$): δ 5.35, bs, 1H; 3.24, q, 2H; 2.02, d, 2H; 1.70, bm, 6H; 1.47, m, 2H; envelope 1.06 - 1.42, 5H; 0.91, m, 5H. MS (DCI-NH_3): 198 (MH^+); 215 ($M+NH_4^+$).



Example 1178F

N-butyl-N-2-cyclohexylethylamine

A stirred suspension of lithium aluminum hydride (23.74 g, 0.63 mol) in THF (400 mL) was cooled in an ice bath and treated with a solution of example 1178E (49.50 g, 0.26 mol) in THF (300 mL). The ice bath was removed and the mixture heated to gentle reflux for 20 hours. The solution was cooled in an ice bath and quenched by the careful addition of 24 mL of water in 100 mL of THF, followed by 24 mL of 15% aqueous sodium hydroxide, followed by an additional 72 mL of water. The thick slurry was vigorously stirred for 15 minutes at which time 600 mL of methylene chloride and excess sodium sulfate were sequentially added. The mixture was stirred for 1 hour and then filtered through celite. The celite pad was washed well with methylene chloride and the filtrate concentrated to give the title compound (47.80 g, 100%) which was sufficiently pure for the next step. ^{1}H nmr (300 MHz., $CDCl_3$): δ 2.61, m, 4H; 1.69, m, 5H; envelope 1.05 - 1.53, 11H; 0.91, m, 5H. MS (DCI-NH_3): 184 (MH^+).

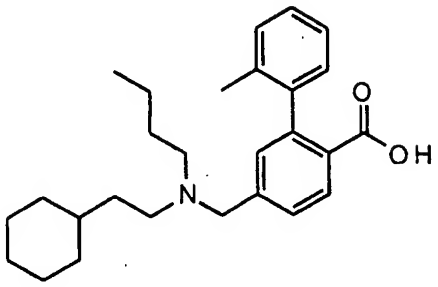


Example 1178G

4-(*N*-(-2-cyclohexylethyl)-*N*-butylaminomethyl)-2-(2-methylphenyl)benzoic acid, methyl ester

A solution of example 1178D (22.2 g, 0.070mol) and diisopropylethylamine (15.7 mL, 0.090 mol) in 100 mL of acetonitrile was treated with N-butyl-N-2-cyclohexylethylamine (15.3 g, 0.084 mol). The cloudy mixture was stirred for two hours and then briefly warmed to ~45°C. After cooling to ambient temperature, the mixture was concentrated to remove the acetonitrile and then diluted with 400 mL of water. The pH of the mixture was brought to >10 with solid potassium phosphate and extracted with 3 portions of ethyl ether. The combined ether extracts were extracted with 1 portion of water and two portions of brine, dried, filtered and concentrated. The residue obtained (34.4 g, 117%) was used directly. An analytical sample was obtained by column chromatography on silica gel (3% ethyl acetate/hexanes) to provide pure material. ^{1}H nmr (300 MHz., $CDCl_3$): δ 7.92, d, 1H; 7.48, dd, 1H; 7.16 - 7.28, m, 4H; 7.07, bd, 1H; 3.62, s, 3H; 3.57, s, 2H; 2.41,

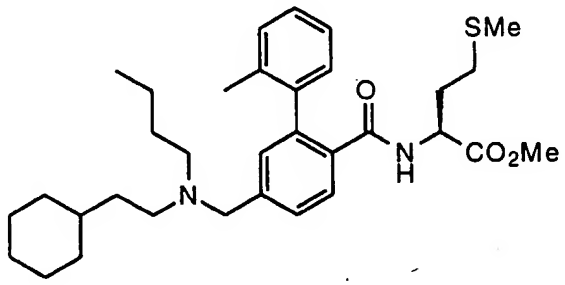
quartet, 4H; 2.06, s, 3H; 1.62, bm, 5H; envelope 1.05 - 1.48, 10H; 0.85, bm, 5H. MS (ESI+): 422 (MH^+): (ESI-): 420 (M-H).



Example 1178H

N-[4-(*N*-(-2-cyclohexylethyl)-*N*-butylaminomethyl)-2-(2-methylphenyl)benzoic acid

A solution of 1178G (34.35 g, 0.081 mol) in 210 mL of ethanol was treated with aqueous sodium hydroxide (4N, 70 mL, 0.28 mol) and the mixture heated to reflux until judged complete by tlc analysis. After cooling to room temperature, the mixture was concentrated to remove the ethanol. The resulting solid was partially dissolved by adding water and the mixture extracted with ethyl ether. The ether layer was then washed with water and then with 1M aqueous phosphoric acid which resulted in an oily precipitate. The precipitate was dissolved by extracting with 3 portions of ethyl acetate and the combined ethyl acetate layer were washed with water, 0.5M aqueous phosphoric acid, brine and then dried, filtered and concentrated to give 24.5 g, (86% yield for the two steps) as a cream colored solid. ^{1}H nmr (300 MHz., CD_3OD): δ 7.96, d, 1H; 7.64, dd, 1H; 7.37, d, 1H; 7.22, m, 2H; 7.18, m, 1H; 7.07, d, 1H; 4.41, bs, 2H; 3.12, m, 4H; 2.10, s, 3H; 1.18, bm, 9H; 1.37, sextet, 2H; 1.23, m, 3H; 0.96, t, 3H; 0.94, m, 2H. MS (ESI+): 408 (MH^+): (ESI-): 406 (M-H).

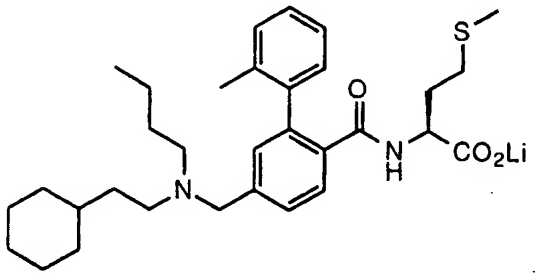


Example 1178I

N-[4-(N-Butyl-N-(2-cyclohexylethyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine methyl ester

Partitioned 13.2 g (66.1 mmol) L-methionine methyl ester, hydrochloride salt between saturated aqueous $NaHCO_3$ (80 mL) and CH_2Cl_2 (75 mL). Added the organic

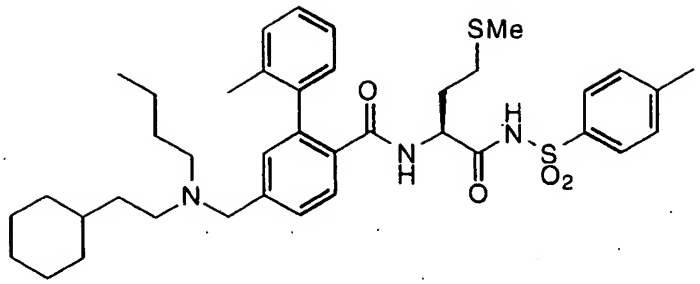
layer to the following solution: 24.5 g (60.2 mmol) acid from Example 1178H, 10.0 g (65.3 mmol) HOBT•H_2O, and 12.6 g (65.7 mmol) EDCI•HCl in DMF (150 mL). After stirring at RT overnight partitioned the reaction between saturated aqueous $NaHCO_3$ (500 mL) and EtOAc (1200 mL). The organic layer was washed with water and brine, then dried over Na_2SO_4. After filtration and concentration, recovered 30 g orange oil that was purified by chromatography using hex/EtOAc 3/1. Recovered 22.9 g (69%) of the title compound. ^1H NMR ($CDCl_3$) δ 7.90 (m, 1H), 7.40 (d, 1H), 7.30, 7.20, 7.16 (all m, total 5H), 5.88 (br d, 1H), 4.62 (m, 1H), 3.66 (s, 3H), 3.57 (s, 2H), 2.41 (m, 4H), 2.18, 2.13, 2.04 (s, m, m, total 9H), 1.85 (m, 1H), 1.62 (m, 5H), 1.50-1.10 (envelope, 10H), 0.87 (m, 5H). MS (APCI) 553 $(M+H)^+$.



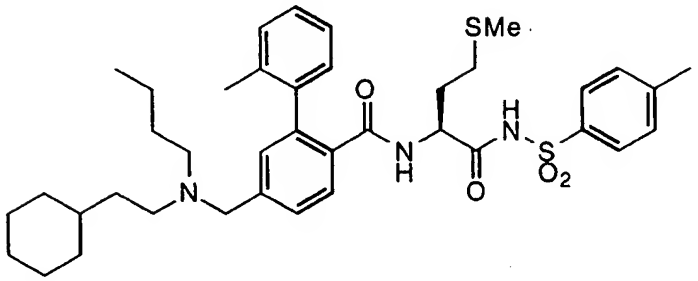
Example 1178J

N-[4-(*N*-(-2-cyclohexylethyl)-*N*-butylaminomethyl)-2-(2-methylphenyl)benzoyl]methionine, Lithium Salt

A solution of example 1178I (22.9 g, 0.041 mol), in 200 mL of 3:1 THF methanol was cooled in an ice bath and then tretaed with aqueous lithium hydroxide (1M, 83 mL, 0.083 mol) dropwise. The ice bath was removed and the mixture was stirred for 20 hours. The solution was concentrated to remove the organics and the resulting thick slurry diluted with water until a clear solution resulted (~1.2 L). The pH of the solution was carefully adjusted to pH~5 with 1M aqueous phosphoric acid and stirred for 1 hour. The solid was collected by filtration and dried under vacuum over phosphorous pentoxide to provide 19.93 g of a cream colored solid. This material was dissolved in 200 mL of THF and treated with a solution of 1.55 g (0.037 mol) of lithium hydroxide in 75 mL of water. The mixture was stirred for 15 minutes and the THF removed under vacuum on a rotary evaporator. The mixture was diluted with 500 mL of water and lyophilized to give 20.10 g (89% overall) of the title compound. ^1H nmr (300 MHz., CD_3OD): δ 7.64, m, 1H; 7.41, d, 1H; 7.05 - 7.32, m, 5H; 4.25, m, 1H; 3.69, s, 2H; 2.52, m, 4H; 2.51, s, 1.5H (1/2 o-tolyl); 2.06, s, 1.5 H (1/2 o-tolyl); 1.98, s, 3H; 1.97, m, 1H; 1.73, m, 2H; 1.64, bm, 6H; envelope 1.04 - 1.56, 10H; 0.90, m, 5H. MS (ESI+): 539 (MH^+): (ESI-): 537 (M-H). Calc'd for $C_{32}H_{45}N_2O_3SLi$•0.60 H_2O; C 69.19; H 8.38; N 5.04; Found: C 69.25; H 8.50; N 4.99.



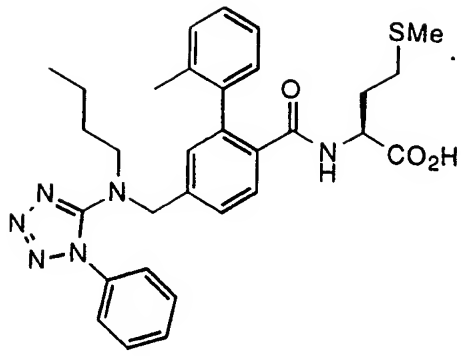
Example 1179



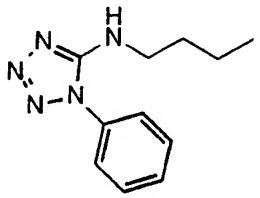
Example 1179

N-[4-N-Butyl-N-(2-cyclohexylethyl)aminomethyl-2-(2-methylphenyl)benzoyl]methionine 4-methylphenylsulfonimide

N-[4-(N-Butyl-N-(2-Cyclohexylethyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine (500 mg, 0.929 mmol), prepared as inExample 1178, p-toluenesulfonamide (429 mg, 2.51 mmol), 4-dimethylaminopyridine (57 mg, 0.465 mmol), and 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide (214 mg, 1.12 mmol) were dissolved in CH_2Cl_2 (10 mL) at room temperature and stirred overnight. Reaction diluted with water and $CHCl_3$ and layers separated. Aqueous layer extracted with $CHCl_3$ (2x), and combined extracts dried with Na_2SO_4, filtered, and concentrated in vacuo. Residue purified by flash chromatography on silica gel eluting with 300:1 EtOAc/25:1:1 EtOAc, H_2O, AcOH to afford the desired compound as a white solid (284 mg, 44%). ^1H (300MHz, MeOD, δ) (rotamer) 7.73 (2H, d, J=9Hz), 7.62 (1H, d, J=8Hz), 7.48 (1H, bd, J=8Hz), 7.30-7.00 (7H, m), 4.22 (1H, m), 4.02 (2H, bs), 2.81 (4H, m), 2.39 (3H, s), 2.21(2.03) (3H, bs), 1.90 (3H, s), 1.85-1.40 (13H, m), 1.40-1.10 (6H, m), 0.93 (5H, t, J=8Hz). m/e (ESI) 690 (MH^-) Anal.calc. for $C_{39}H_{53}N_3O_4S_2 \cdot 1.25\ H_2O$ C 65.56, H 7.83, N 5.88 Found C 65.41, H 7.52, N 5.61



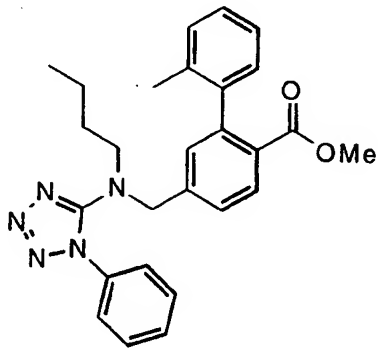
Example 1180



Example 1180A

N-Butyl-N-(1-phenyltetrazol-5-yl)amine

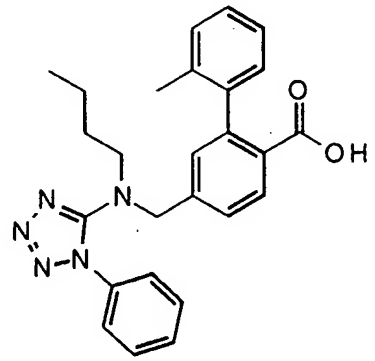
5-Chloro-1-phenyl-1H-tetrazole (1.00 g, 5.54 mmol), butylamine (0.547 mL, 5.54 mmol), and diisopropylethylamine (1.48 mL, 8.31 mmol) were dissolved in DMF (5 mL), and stirred overnight at room temperature. Reaction diluted with EtOAc and washed with water and brine. Organic layer dried with Na_2SO_4, filtered, and concentrated in vacuo. Residue purified by flash chromatography on silica gel eluting with 35% EtOAc/Hexanes to afford the desired product as a white solid (625 mg, 52%). m/e (DCI) 218 (MH^+)



Example 1180B

4-N-Butyl-N-(1-phenyltetrazol-5-yl)aminomethyl-2-(2-methylphenyl)benzoic acid methyl ester

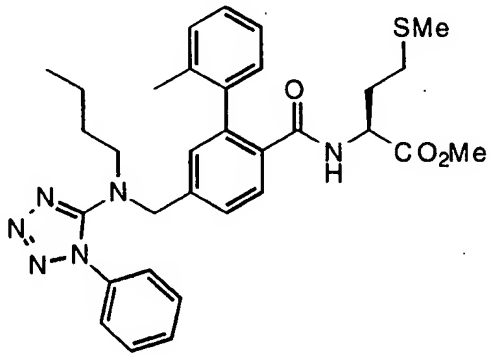
The desired compound was prepared according to the method of Example 1174B starting with 4-bromomethyl-2-(2-methylphenyl)benzoic acid methyl ester, prepared as in Example 1178A-D, and the compound from Example 1180A.



Example 1180C

4-N-Butyl-N-(1-phenyltetrazol-5-yl)aminomethyl-2-(2-methylphenyl)benzoic acid

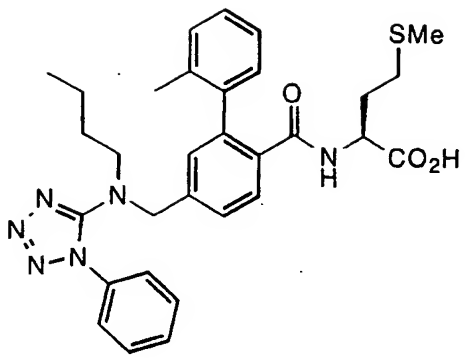
The desired acid was prepared using the method described inExample 403E starting with the product fromExample 1180B. m/e (ESI) 440 (MH^-)



Example 1180D

N-[4-N-Butyl-N-(1-phenyltetrazol-5-yl)aminomethyl-2-(2-methylphenyl)benzoyl]methionine methyl ester

The desired compound was prepared using the method described inExample 403F starting with the product fromExample 1180C. m/e (ESI) 587 (MH^+)



13975

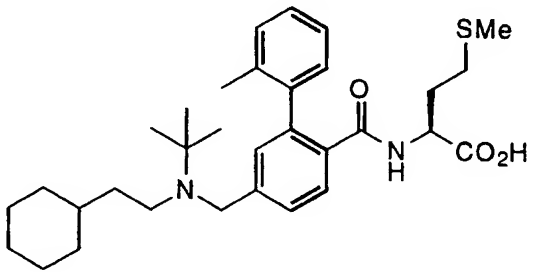
Example 1180E

N-[4-N-Butyl-N-(1-phenyltetrazol-5-yl)aminomethyl-2-(2-methylphenyl)benzoyl]methionine

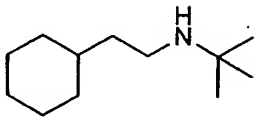
The desired compound was prepared according to the method ofExample 403I starting with the compound fromExample 1180D. ^1H (300MHz, $CDCl_3$, δ) 7.93 (1H, m),

13980 7.60-7.40 (5H, m), 7.40-7.10 (5H, m), 7.03 (1H, d, J=2Hz), 5.89 (1H, m), 4.55 (1H, m), 4.52 (2H, s), 3.11 (2H, bt, J=8Hz), 2.20-2.00 (8H, m), 1.90 (1H, m), 1.56 (1H, m), 1.43 (2H, m), 1.06 (2H, m), 0.74 (3H, t, J=8Hz). m/e (ESI) 571 (MH^+) Anal.calc. for $C_{31}H_{36}N_6O_3S$ C 65.01, H 6.34, N 14.67 Found C 64.77, H 6.33, N 14.70

13985



Example 1181

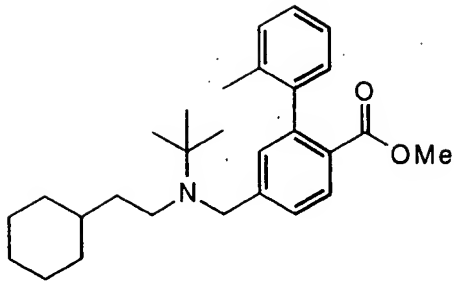


13990

Example 1181A

N-t-Butyl-N-(2-cyclohexylethyl)amine

The desired amine was prepared using the method described inExample 1171A starting with cyclohexylacetic acid and t-butylamine. m/e (DCI/NH_3) 184 (MH^+)

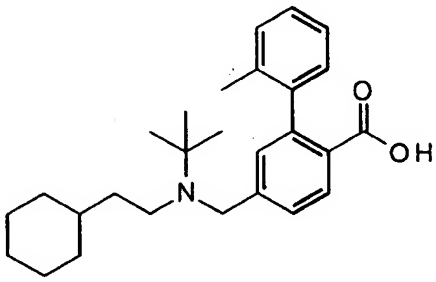


13995

Example 1181B

4-(N-t-Butyl-N-(2-cyclohexylethyl)aminomethyl)-2-(2-methylphenyl)benzoic acid methyl ester

The desired compound was prepared using the method described inExample 1178G
14000 starting with N-t-butyl-N-(2-cyclohexylethyl)amine, prepared as inExample 1181A, and 4-bromomethyl-2-(2-methylphenyl)benzoic acid methyl ester, prepared as inExample 1178A-D. m/e (ESI) 422 (MH^+)

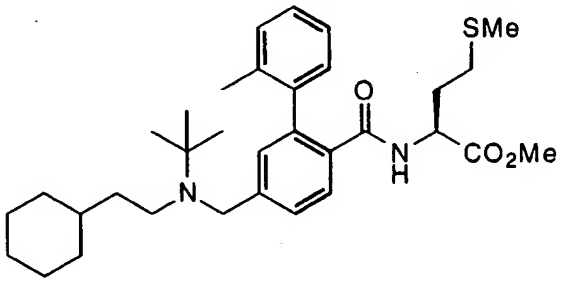


14005

Example 1181C

4-(N-t-Butyl-N-(2-cyclohexylethyl)aminomethyl)-2-(2-methylphenyl)benzoic acid

The desired acid was prepared using the method described in Example 403E starting with the compound prepared in Example 1181B.

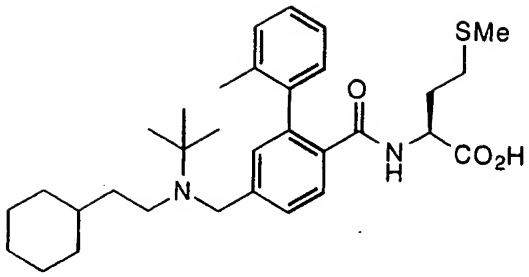


14010

Example 1181D

N-[4-N-t-Butyl-N-(2-cyclohexylethyl)aminomethyl-2-(2-methylphenyl)benzoyl]methionine methyl ester

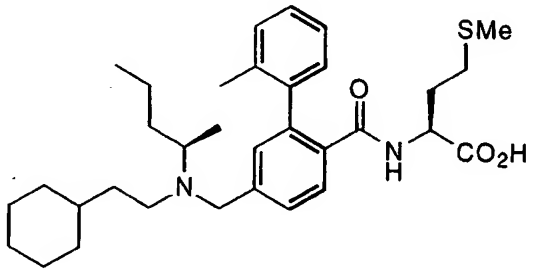
The desired product was prepared using the method described inExample 403F
14015 starting with the compound prepared inExample 1181C. m/e (ESI) 553 (MH^+)



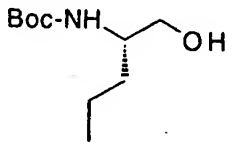
Example 1181E

N-[4-N-t-Butyl-N-(2-cyclohexylethyl)aminomethyl-2-(2-methylphenyl)benzoyl]methionine

The desired compound was prepared according to the method ofExample 403I starting with compound prepared inExample 1181D.^{1}H (300MHz, $CDCl_3$, δ) 7.78 (1H, m), 7.67 (1H, m), 7.40-7.00 (5H, m), 6.21 (1H, m), 4.38 (1H, m), 4.13 (2H, m), 2.93 (2H, m), 2.20-2.00 (7H, m), 2.00 (3H, s), 1.60 (4H, m), 1.43 (12H, bs), 1.40-0.90 (4H, m), 0.75 (2H, m). m/e (ESI) 537 (MH^+) Anal.calc. for $C_{32}H_{46}N_2O_3S \cdot 0.75\ H_2O$ C 69.59, H 8.67, N 5.07 Found C 69.78, H 8.65, N 4.89



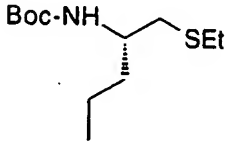
Example 1182



Example 1182A

(2S)-t-Butoxycarbonylaminopentan-1-ol

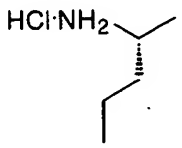
The desired product was prepared using the methods described in Example 1183A starting with L-norvaline.



Example 1182B

(2S)-t-Butoxycarbonylamino-1-ethylthiopentane

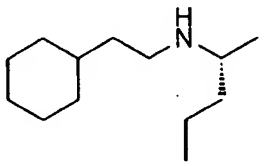
The desired product was prepared using the methods described in Example 403B and 403C starting with the compound prepared in Example 1182A.



Example 1182C

(2R)-Aminopentane hydrochloride salt

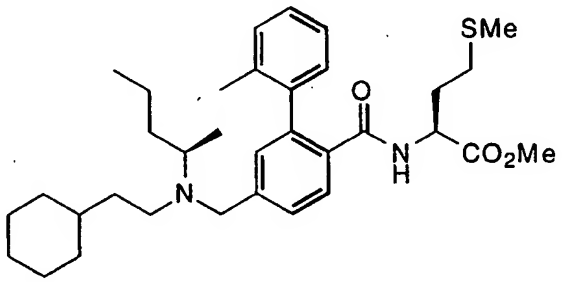
The desired product was prepared using the methods described in Example 1183C starting with the compound prepared in Example 1182B.



Example 1182D

N-(2-Cyclohexylethyl)-N-(pent-2-yl)amine

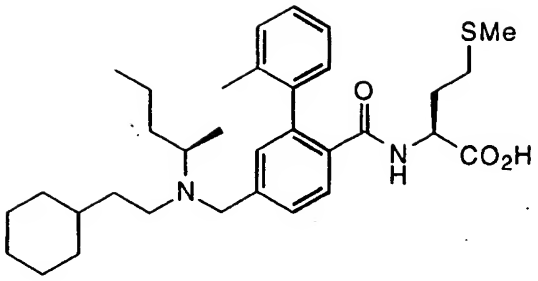
The desired amine was prepared using the method described inExample 1171A, except triethylamine was added, starting with cyclohexylacetic acid and the compound fromExample 1182C. m/e (DCI) 198 (MH^+)



Example 1182E

N-[4-N-(2-Cyclohexylethyl)-N-(pent-2-yl)aminomethyl-2-(2-methylphenyl)benzoyl]methionine methyl ester

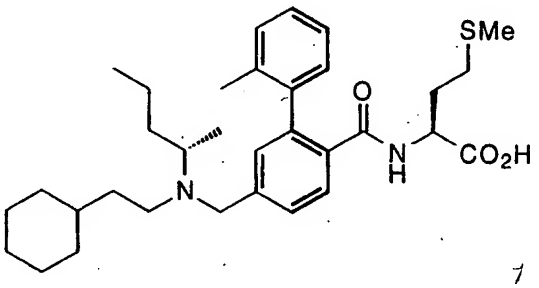
The desired product was prepared using the method described inExample 403H starting with the compound prepared inExample 1182D and N-[4-formyl-2-(2-methylphenyl)benzoyl]methionine methyl ester, prepared as inExample 403G. m/e (ESI) 567 (MH^+)



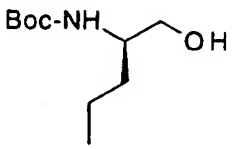
Example 1182F

N-[4-N-(2-Cyclohexylethyl)-N-(pent-2-yl)aminomethyl-2-(2-methylphenyl)benzoyl]methionine

The desired compound was prepared according to the method ofExample 403I starting with the compound prepared inExample 1182E. ^{1}H (300MHz, $CDCl_3$, δ) 7.74 (1H, m), 7.62 (1H, m), 7.40-7.00 (5H, m), 6.46 (1H, m), 4.37 (1H, m), 3.94 (2H, m), 3.37 (1H, m), 2.90 (2H, m), 2.20-1.80 (8H, m), 1.80-1.60 (6H, m), 1.55-1.25 (6H, m), 1.25-1.00 (8H, m), 0.91 (3H, t, J=8Hz), 0.82 (2H, m). m/e (ESI) 551 (MH^-) Anal.calc. for $C_{33}H_{48}N_2O_3S \cdot 0.50\ H_2O$ C 70.55, H 8.79, N 4.99 Found C 70.55, H 8.71, N 4.87



Example 1183

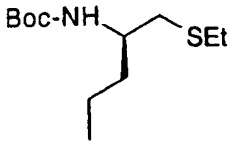


Example 1183A

(2R)-t-Butoxycarbonylaminopentan-1-ol

To a stirred solution at ambient temperature of D-norvaline (5.00 g, 42.7 mmol) in THF (100 mL) was added an aqueous 4N NaOH solution (21 mL, 84 mmol), di-t-butyl dicarbonate (11.2 g, 51.2 mmol), and tetrabutylammonium bromide (1.0 g). Two-phase solution stirred overnight at ambient temperature. Reaction neutralized with aqueous 3N HCl to pH 6 and extracted with $CHCl_3$ (3x). Extracts dried with Na_2SO_4, filtered, and concentrated in vacuo to produce a colorless oil. To a stirred solution at 0°C under N_2 of the

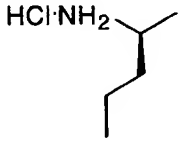
crude residue in anhydrous THF (80 mL) was added dropwise via addition funnel a 1.0M borane-THF complex (100 mL, 100 mmol) in THF. After stirring overnight at ambient temperature, reaction cooled back to 0°C and quenched with an aqueous 4N NaOH solution (50 mL). Mixture stirred one hour at ambient temperature, and then, extracted with CH_2Cl_2 (3x). Extracts dried with Na_2SO_4, filtered, and concentrated in vacuo. Residue purified by flash chromatography on silica gel eluting with 30% EtOAc/Hexanes to afford the alcohol as a pale yellow oil (3.87 g, 45%). m/e (DCI) 204 (MH^+)



Example 1183B

(2R)-t-Butoxycarbonylamino-1-ethylthiopentane

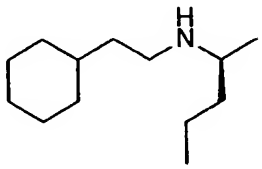
The desired product was prepared using the methods described in Example 403B and 403C starting with the compound prepared in Example 1183A. m/e (DCI) 248 (MH^+)



Example 1183C

(2S)-Aminopentane hydrochloride salt

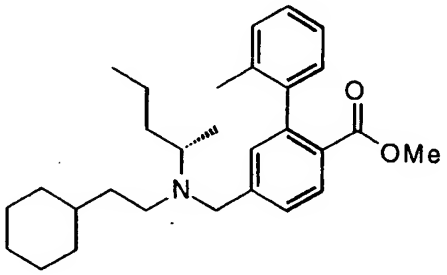
To a stirred solution at ambient temperature of (2R)-t-butoxycarbonylamino-1-ethylthiopentane (655 mg, 2.65 mmol), prepared as in Example 1183B, in EtOH (5 mL) was added a 50% slurry of Raney Nickel (2.65 g) in water. Mixture stirred vigorously at 80°C for 2 days. Reaction filtered through celite, and celite and catalyst washed with EtOAc. Filtrate concentrated in vacuo to produce a colorless liquid. Residue taken up in a solution of 4N HCl in dioxane (5 mL), and reaction stirred overnight at ambient temperature. Ether added until a solid precipitated. Solid filtered off, washed with ether, and dried to produce the desired compound as a white solid (167 mg, 59%).



Example 1183D

N-(2-Cyclohexylethyl)-N-(pent-2-yl)amine

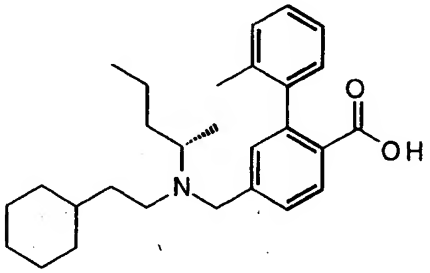
The desired amine was prepared using the method described in Example 1171A, except triethylamine was added, starting with cyclohexylacetic acid and the compound from Example 1183C. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 2.70-2.50 (m, 4H), 1.80-1.60 (m, 6H), 1.50-1.00 (m, 8H), 1.04 (d, 3H, J=8Hz), 1.00-0.80 (m, 5H)



Example 1183E

N-[4-N-(2-Cyclohexylethyl)-N-(pent-2-yl)aminomethyl-2-(2-methylphenyl)benzoic acid methyl ester

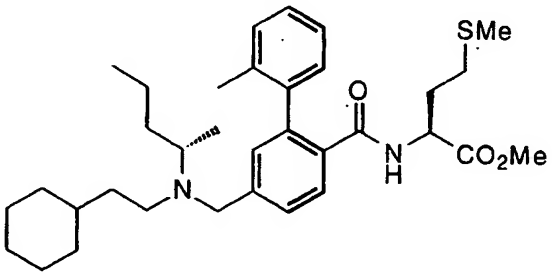
The desired compound was prepared using the method described in Example 1178G starting with N-(2-cyclohexylethyl)-N-(1-methylbutyl)amine, prepared as in Example 1183D, and 4-bromomethyl-2-(2-methylphenyl)benzoic acid methyl ester, prepared as in Example 1178A-D. m/e (ESI) 436 (MH^+)



Example 1183F

N-[4-N-(2-Cyclohexylethyl)-N-(pent-2-yl)aminomethyl-2-(2-methylphenyl)benzoic acid

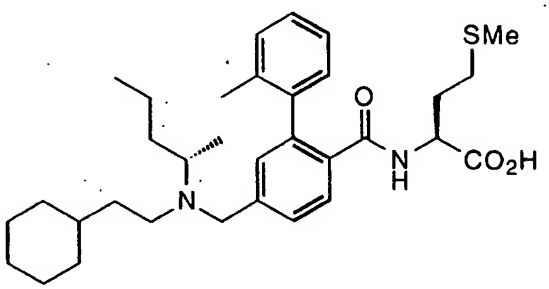
The desired acid was prepared using the method described in Example 403E starting with the compound prepared in Example 1183E.



Example 1183G

N-[4-N-(2-Cyclohexylethyl)-N-(pent-2-yl)aminomethyl-2-(2-methylphenyl)benzoyl]methionine methyl ester

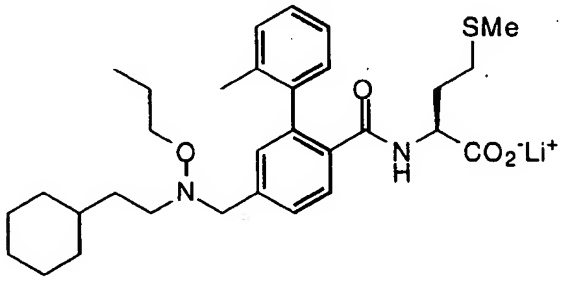
The desired product was prepared using the method described in Example 403F starting with the compound prepared in Example 1183F. m/e (ESI) 567 (MH^+)



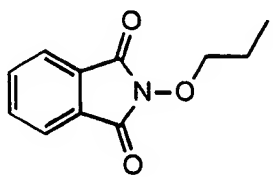
Example 1183H

N-[4-N-(2-Cyclohexylethyl)-N-(pent-2-yl)aminomethyl-2-(2-methylphenyl)benzoyl]methionine

The desired compound was prepared according to the method of Example 403I starting with the compound from Example 1183G. ^1H (300MHz, $CDCl_3$, δ) 7.69 (2H, m), 7.40-7.00 (5H, m), 6.46 (1H, m), 4.38 (1H, m), 4.05 (2H, m), 3.41 (1H, m), 2.90 (2H, m), 2.20-1.75 (9H, m), 1.75-1.50 (7H, m), 1.50-1.00 (12H, m), 0.90 (5H, m). m/e (ESI) 551 (MH^-) Anal.calc. for $C_{33}H_{48}N_2O_3S \cdot 0.50\ H_2O$ C 70.55, H 8.79, N 4.99 Found C 70.65, H 8.63, N 4.93



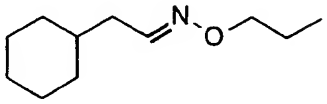
Example 1184



Example 1184A

N-Propoxyphthalimide

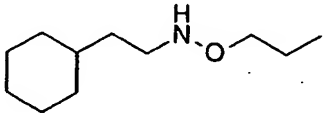
The desired product was prepared using the method described in Example 1176A starting with N-hydoxyphthalimide and 1-propanol. m/e (DCI) 223 ($MH+NH_3^+$)



Example 1184B

O-Propyl-2-cyclohexylacetaldoxime

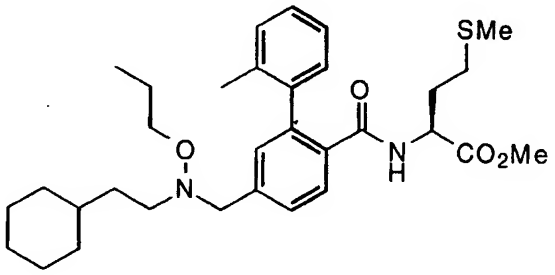
The desired product was prepared using the method described in Example 1176B starting with the compound from Example 1184 A and cyclohexylacetaldehyde.



Example 1184C

N--(2-Cyclohexylethyl)-N-propyloxyamine

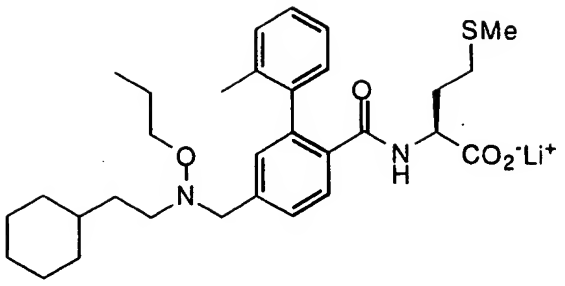
The desired product was prepared using the method described in Example 1176C starting with the compound from Example 1184B. m/e (DCI) 186 (MH^+)



Example 1184D

N-[4-N--(2-Cyclohexylethyl)-N-propyloxyaminomethyl-2-(2-methylphenyl)benzoyl]methionine methyl ester

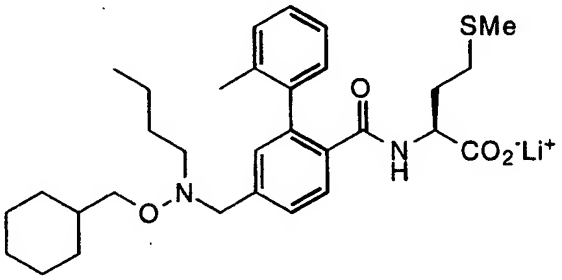
The desired product was prepared using the method described in Example 403H starting with the compound from Example 1184C and N-[4-Formyl-2-(2-methylphenyl)benzoyl]methionine methyl ester, prepared as in Example 403G. m/e (ESI) 553 (MH^-)



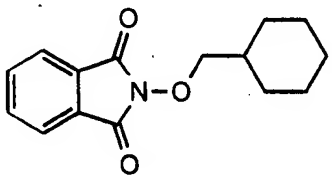
Example 1184E

N-[4-N--(2-Cyclohexylethyl)-N-propyloxyaminomethyl-2-(2-methylphenyl)benzoyl]methionine lithium salt

The desired compound was prepared according to the method of Example 403I starting with th compound from Example 1184D. ^1H (300MHz, DMSO-d6, δ) 7.53 (1H, d, J=9Hz), 7.38 (1H, dd, J=7&2Hz), 7.30-7.00 (5H, m), 6.92 (1H, m), 3.82 (2H, bs), 3.71 (1H, m), 3.41 (2H, m), 2.67 (2H, bt, J=8Hz), 2.25-1.95 (5H, m), 1.91 (3H, s), 1.90-1.50 (7H, m), 1.37 (5H, m), 1.15 (3H, m), 0.86 (2H, m), 0.76 (3H, t, J=8Hz). m/e (ESI) 539 (MH^-) Anal.calc: for $C_{31}H_{43}LiN_2O_4S \cdot 0.50\ H_2O$ C 67.00, H 7.98, N 5.04 Found C 66.82, H 7.75, N 4.92.



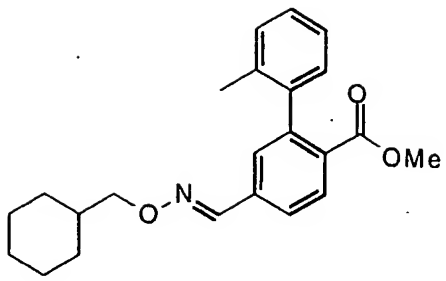
Example 1185



Example 1185A

N-Cyclohexylmethoxyphthalimide

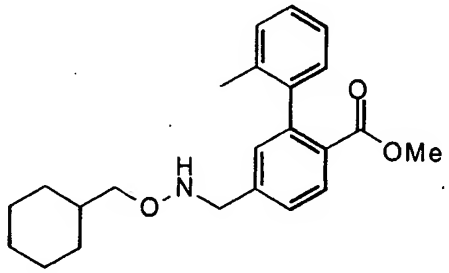
The desired product was prepared using the method described in Example 1176A starting with N-hydoxyphthalimide and cyclohexylmethanol.



Example 1185B

N-(Cyclohexylmethyloxy)aminomethylidene-2-(2-methylphenyl)benzoic acid methyl ester

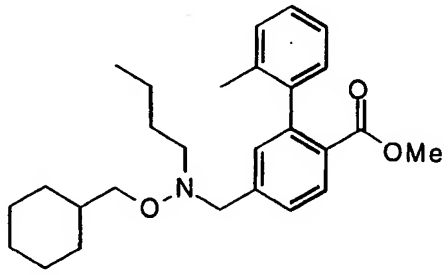
The desired product was prepared using the method described in Example 1176B starting with the compound from Example 1185A and *N*-[4-Formyl-2-(2-methylphenyl)benzoic acid methyl ester, prepared using the method of Example 403G and starting with the alcohol prepared in Example 1178C.



Example 1185C

N-(Cyclohexylmethyloxy)aminomethyl-2-(2-methylphenyl)benzoic acid methyl ester

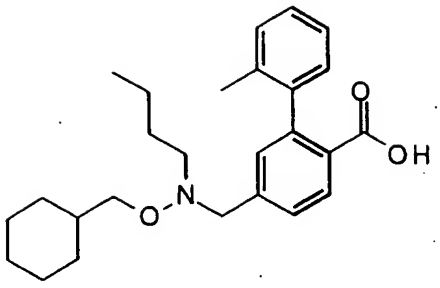
The desired product was prepared using the method described in Example 1176C starting with the compound in Example 1185B. m/e (ESI) 368 (MH^+)



Example 1185D

N-[4-*N*--Butyl-*N*-(cyclohexylmethyloxy)aminomethyl-2-(2-methylphenyl)benzoic acid methyl ester

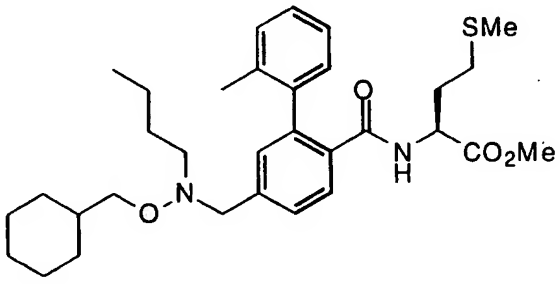
The desired product was prepared using the method described in Example 1176D starting with the compound in Example 1185C. m/e (ESI) 424 (MH^+)



Example 1185E

N-[4-*N*--Butyl-*N*-(cyclohexylmethyloxy)aminomethyl-2-(2-methylphenyl)benzoic acid

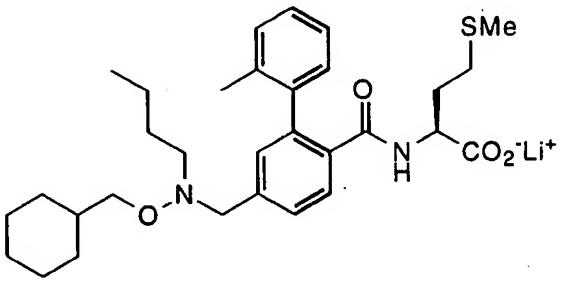
The desired product was prepared using the method described in Example 403E starting with the compound in Example 1185D.



Example 1185F

N-[4-*N*--Butyl-*N*-(cyclohexylmethyloxy)aminomethyl-2-(2-methylphenyl)benzoyl]methionine methyl ester

The desired product was prepared using the method described in Example 403F starting with the compound in Example 1185E. m/e (ESI) 555 (MH^+)



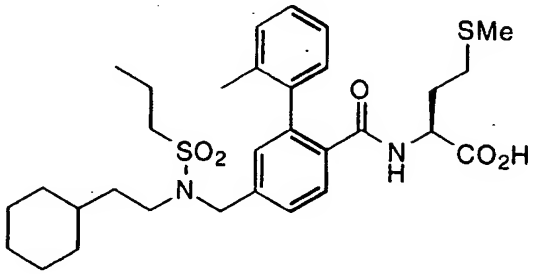
Example 1185G

N-[4-*N*--Butyl-*N*-(cyclohexylmethyloxy)aminomethyl-2-(2-methylphenyl)benzoyl]methionine lithium salt

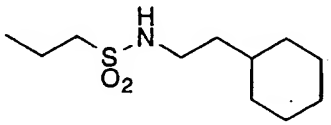
The desired compound was prepared according to the method of Example 403I starting wiyh the compound in Example 1185F. ^1H (300MHz, DMSO-d6, δ) 7.51 (1H, d, J=9Hz), 7.37 (1H, bd), 7.30-7.05 (5H, m), 6.94 (1H, m), 3.82 (2H, bs), 3.68 (1H, m), 3.25 (2H, m), 2.64 (2H, t, J=8Hz), 2.25-1.95 (5H, m), 1.93 (3H, s), 1.90-1.40 (9H, m),

1.31 (3H, m), 1.06 (3H, m), 0.85 (3H, t, J=8Hz), 0.73 (2H, m). m/e (ESI) 539 (MH^-) Anal.calc. for $C_{31}H_{43}LiN_2O_4S \cdot 2.00\ H_2O$ C 63.90, H 8.13, N 4.81 Found C 63.63, H 7.68, N 4.62

14255



Example 1187

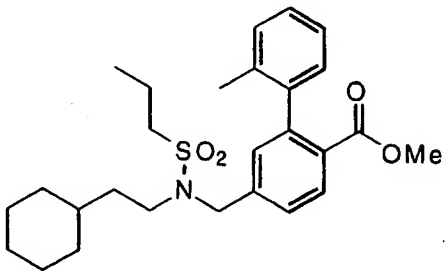


14260

Example 1187A

N-(2-Cyclohexylethyl)-N-propanesulfonylamine

The desired product was prepared using the method described in Example 1174A starting with cyclohexylethylamine and 1-propanesulfonyl chloride.



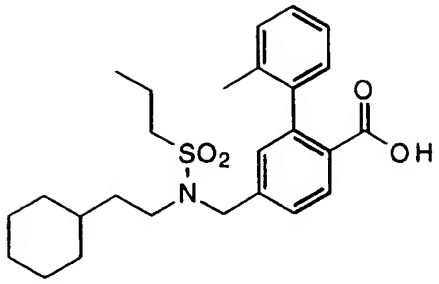
14265

Example 1187B

4-(N-(2-Cyclohexylethyl)-N-propanesulfonylaminomethyl)-2-(2-methylphenyl)benzoic acid methyl ester

The desired product was prepared using the method described inExample 1174B

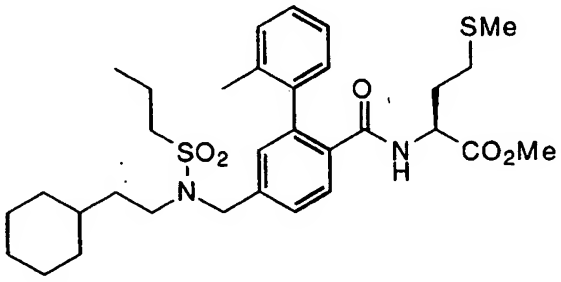
14270 starting with N-(2-cyclohexylethyl)-N-propanesulfonylamine, prepared as inExample 1187A, and 4-bromomethyl-2-(2-methylphenyl)benzoic acid methyl ester, prepared as inExample 1178A-D. m/e (ESI) 472 (MH^+)



Example 1187C

4-(N-(2-Cyclohexylethyl)-N-propanesulfonylaminomethyl)-2-(2-methylphenyl)benzoic acid

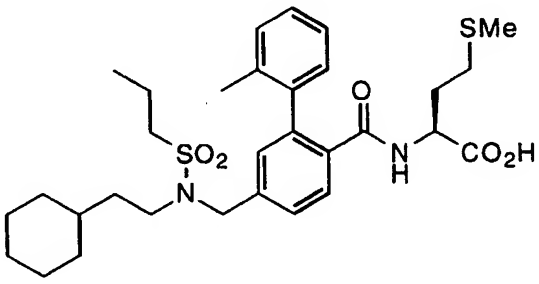
The desired acid was prepared using the method described in Example 403E starting with the product from Example 1187B.



Example 1187D

N-[4-N-(2-Cyclohexylethyl)-N-propanesulfonylaminomethyl-2-(2-methylphenyl)benzoyl]methionine methyl ester

The desired compound was prepared using the method described inExample 403F starting with the product fromExample 1187C. m/e (ESI) 601 (MH^-)

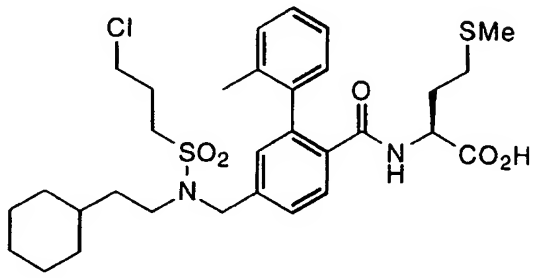


Example 1187E

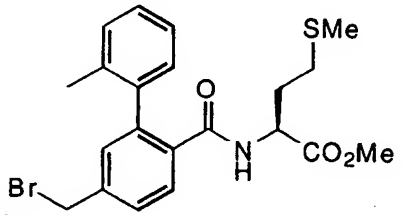
N-[4-N-(2-Cyclohexylethyl)-N-propanesulfonylaminomethyl-2-(2-methylphenyl)benzoyl]methionine

The desired compound was prepared according to the method ofExample 403I starting with the compound prepared inExample 1187D. ^1H (300MHz, $CDCl_3$, δ) 8.00 (1H, dd, J=8&7Hz), 7.43 (1H, dd, J=7&2Hz), 7.40-7.10 (5H, m), 5.90 (1H, m), 4.58 (1H, m), 4.42 (2H, s), 3.20 (2H, m), 2.94 (2H, m), 2.20-2.00 (7H, m), 2.00-1.80 (4H,

m), 1.60 (6H, m), 1.38 (2H, m), 1.15 (4H, m), 1.05 (3H, t, J=8Hz), 0.86 (2H, m). m/e (ESI) 587 (MH^-) Anal.calc. for $C_{31}H_{44}N_2O_5S_2 \cdot 0.25\ H_2O$ C 62.75, H 7.56, N 4.72 Found C 62.75, H 7.56, N 4.49



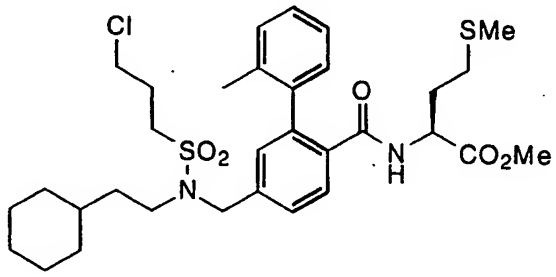
Example 1188



Example 1188A

N-[Bromomethyl-2-(2-methylphenyl)benzoyl]methionine methyl ester

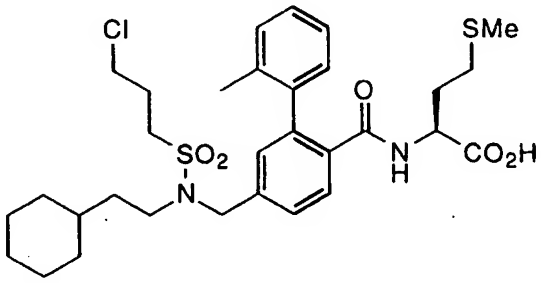
To a stirred solution at -10°C under N_2 of N-[4-hydroxymethyl-2-(2-methylphenyl)benzoyl]methionine methyl ester (200 mg, 0.517 mmol), prepared as in Example 403F, and carbon tetrabromide (189 mg, 0.568 mmol) in CH_2Cl_2 (5 mL) was added triphenylphosphine (163 mg, 0.620 mmol). Reaction stirred one hour at -10°C, and then, solvents concentrated in vacuo to produce a colorless glass. The residue could not be stored, and so, was used directly in the reaction in Example 1188B.



Example 1188B

N-[4-N-(3-Chloropropanesulfonyl)-N-(2-cyclohexylethyl)aminomethyl-2-(2-methylphenyl)benzoyl]methionine methyl ester

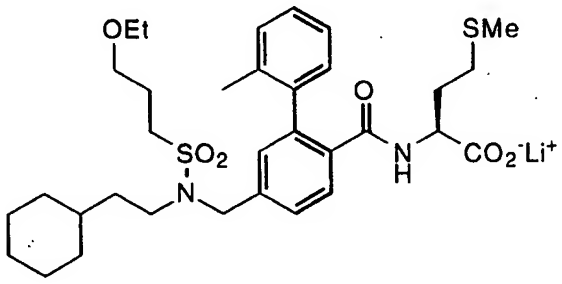
The desired compound was prepared using the method described in Example 1174B (except reaction run at -40°C) starting with the product from Example 1188A and N-(3-chloropropanesulfonyl)-N-(2-cyclohexylethyl)amine, prepared as in Example 1189A using the method described in Example 1174A. m/e (ESI) 635 (MH^-)



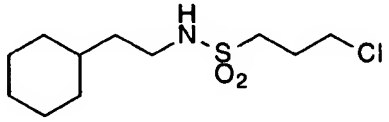
Example 1188C

N-[4-N-(3-Chloropropanesulfonyl)-N-(2-cyclohexylethyl)aminomethyl-2-(2-methylphenyl)benzoyl]methionine

The desired compound was prepared according to the method of Example 403I starting with the compound from Example 1188B. ^1H (300MHz, $CDCl_3$, δ) 8.01 (1H, bt, J=8Hz), 7.46 (1H, dd, J=7&2Hz), 7.40-7.10 (5H, m), 5.90 (1H, m), 4.59 (1H, m), 4.45 (2H, s), 3.68 (2H, t, J=8Hz), 3.22 (2H, bt, J=7Hz), 3.12 (2H, t, J=8Hz), 2.31 (2H, m), 2.20-2.05 (4H, m), 2.03 (3H, s), 1.92 (2H, m), 1.60 (6H, m), 1.40 (2H, m), 1.30-1.00 (4H, m), 0.85 (2H, m). m/e (ESI) 621 (MH^-) Anal.calc. for $C_{31}H_{43}Cl_1N_2O_5S_2 \cdot 0.50\ H_2O$ C 58.89, H 7.01, N 4.43 Found C 58.96, H 7.04, N 4.40



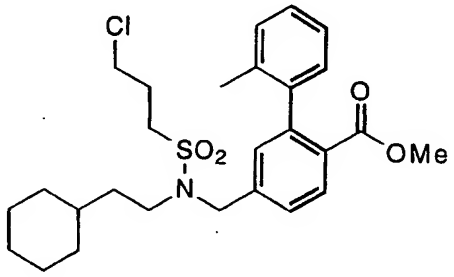
Example 1189



Example 1189A

N-(3-Chloropropanesulfonyl)-N-(2-cyclohexylethyl)amine

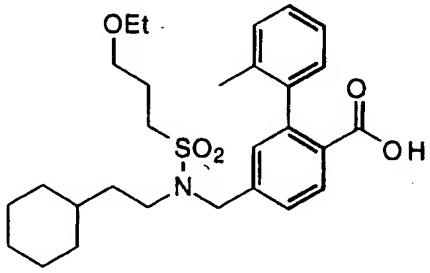
The desired compound was prepared using the method described in Example 1174A starting with cyclohexylethylamine and 3-chloropropanesulfonyl chloride.



Example 1189B

4-N-(3-Chloropropanesulfonyl)-N-(2-cyclohexylethyl)aminomethyl-2-(2-methylphenyl)benzoic acid methyl ester

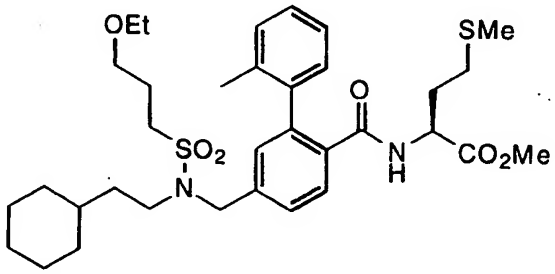
The desired product was prepared using the method described inExample 1174B starting with the compound fromExample 1189A and 4-bromomethyl-2-(2-methylphenyl)benzoic acid methyl ester, prepared as inExample 1178A-D. m/e (ESI) 506 (MH^+)



Example 1189C

N-[4-N-(2-Cyclohexylethyl)-N-(3-ethoxypropanesulfonyl)aminomethyl-2-(2-methylphenyl)benzoic acid

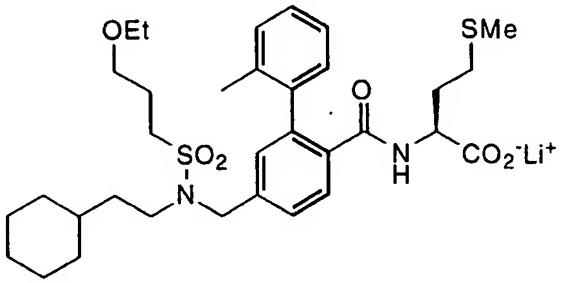
The acid was prepared using the method described in Example 403E starting with the product from Example 1189B. Chloride was displaced by ethoxide ion.



Example 1189D

N-[4-N-(2-Cyclohexylethyl)-N-(3-ethoxypropanesulfonyl)aminomethyl-2-(2-methylphenyl)benzoyl]methionine methyl ester

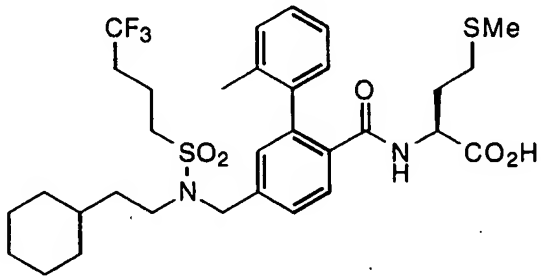
The compound was prepared using the method described in Example 403F starting with the product from Example 1189C. m/e (ESI) 645 (MH^-)



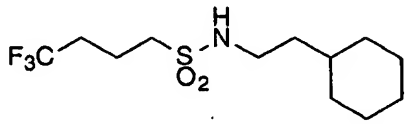
Example 1189E

N-[4-N-(2-Cyclohexylethyl)-N-(3-ethoxypropanesulfonyl)aminomethyl-2-(2-methylphenyl)benzoyl]methionine lithium salt

The desired compound was prepared according to the method of Example 403I starting with the compound from Example 1189D. ^1H (300MHz, DMSO-d6, δ) 7.54 (1H, d, J=8Hz), 7.41 (1H, dd, J=7&2Hz), 7.30-7.10 (5H, m), 6.97 (1H, d, J=7Hz), 4.42 (2H, bs), 3.68 (1H, m), 3.43 (2H, q, J=7Hz), 3.40 (2H, m), 3.16 (4H, m), 2.20-1.95 (5H, m), 1.95 (3H, s), 1.90-1.65 (3H, m), 1.55 (6H, m), 1.27 (2H, m), 1.10 (7H, bt, J=8Hz), 0.78 (2H, m). m/e (ESI) 631 (MH^-) Anal.calc. for $C_{33}H_{47}LiN_2O_6S_2 \cdot 0.50\ H_2O$ C 61.18, H 7.47, N 4.32 Found C 61.15, H 7.53, N 4.15



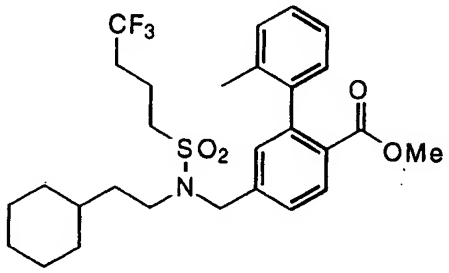
Example 1190



Example 1190A

N-(2-Cyclohexylethyl)-N-(3-trifluoromethylpropanesulfonyl)amine

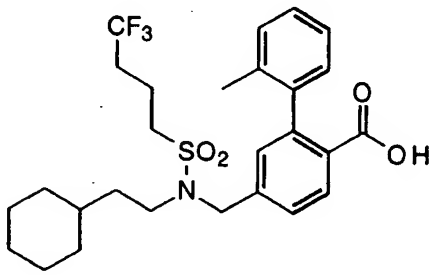
To a stirred solution at 0°C under N_2 of 4,4,4-trifluoro-1-bromobutane (2.00 g, 10.5 mmol) in anhydrous DMF (10 mL) was added dropwise a slurry of t-butanethiol sodium salt (1.29 g, 11.5 mmol) in anhydrous DMF (25 mL) such that the temperature was maintained below 5°C. Mixture stirred one hour at 0°C, and then, diluted with water and extracted with ether. Extracts dried with Na_2SO_4, filtered, and concentrated in vacuo. Residue dissolved in 1:1 water/EtOH at 0°C, and to this was bubbled in chlorine gas for 45 minutes. After the chlorine addition, N_2 was bubbled into the black-green mixture until the green color disappeared (30 minutes). The mixture was made a more homogeneous solution by addition of CH_2Cl_2, and to this was added carefully an aqueous 2M Na_2CO_3 solution until mixture was basic (pH 10). Cyclohexylethylamine (1.14 g, 9.00 mmol) was added, and this two-phase solution was stirred at room temperature overnight. Reaction diluted with water and extracted with $CHCl_3$ (2x). Extracts dried with Na_2SO_4, filtered, and concentrated. Residue purified by flash chromatography on silica gel eluting with 20% EtOAc/Hexanes to afford the desired product as a light brown oil (1.02 g, 32%). m/e (DCI) 319 ($MH+NH_3^+$)



Example 1190B

4-(N-(2-Cyclohexylethyl)-N-(3-trifluoromethylpropanesulfonyl)aminomethyl)-2-(2-methylphenyl)benzoic acid methyl ester

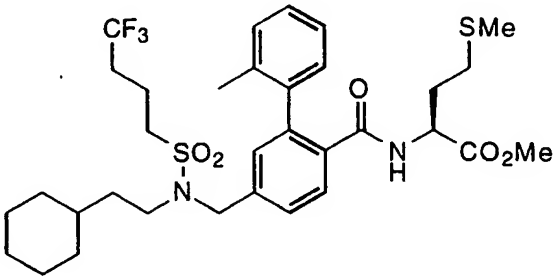
The desired product was prepared using the method described in Example 1174B starting with N-(2-cyclohexylethyl)-N-(3-trifluoromethylpropanesulfonyl)amine, prepared as in Example 1190A, and 4-bromomethyl-2-(2-methylphenyl)benzoic acid methyl ester, prepared as in Example 1178A-D.



Example 1190C

4-(N-(2-Cyclohexylethyl)-N-(3-trifluoromethylpropanesulfonyl)aminomethyl)-2-(2-methylphenyl)benzoic acid

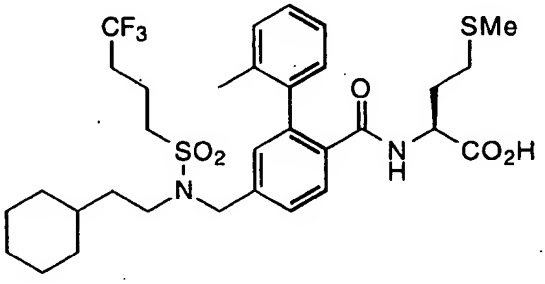
The desired acid was prepared using the method described in Example 403E starting with the product from Example 1190B. m/e (ESI) 524 (MH^-)



Example 1190D

N-[4-N-(2-Cyclohexylethyl)-N-(3-trifluoromethylpropanesulfonyl)aminomethyl-2-(2-methylphenyl)benzoyl]methionine methyl ester

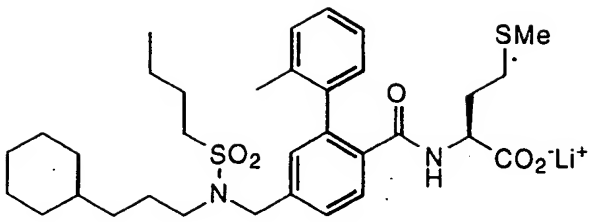
The desired compound was prepared using the method described in Example 403F starting with the product from Example 1190C. m/e (ESI) 669 (MH^-)



Example 1190E

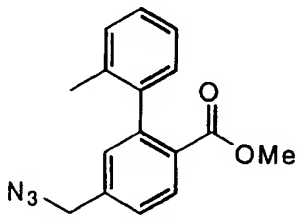
N-[4-N-(2-Cyclohexylethyl)-N-(3-trifluoromethylpropanesulfonyl)aminomethyl-2-(2-methylphenyl)benzoyl]methionine

The desired compound was prepared according to the method of Example 403I starting with the compound in Example 1190D. ^1H (300MHz, $CDCl_3$, δ) (rotamer) 8.01(7.98) (1H, d, J=8Hz), 7.46 (1H, dd, J=7&2Hz), 7.40-7.10 (5H, m), 5.92 (1H, m), 4.80 (1H, bs), 4.58 (1H, m), 4.45 (2H, s), 3.22 (2H, bt, J=7Hz), 3.03 (2H, t, J=8Hz), 2.30 (2H, m), 2.20-2.00 (10H, m), 1.92 (1H, m), 1.62 (6H, m), 1.40 (2H, m), 1.30-1.00 (4H, m), 0.87 (2H, m). m/e (ESI) 655 (MH^-) Anal.calc. for $C_{32}H_{43}F_3N_2O_5S_2$ C 58.52, H 6.60, N 4.26 Found C 58.27, H 6.63, N 4.13



Example 1191

14440



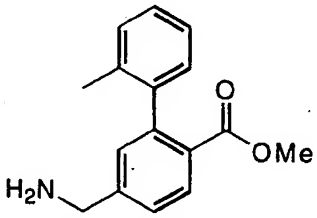
Example 1191A

4-Azidomethyl-2-(2-methylphenyl)benzoic acid methyl ester

To a stirred mixture at 0°C under N_2 of sodium azide (1.47 g, 22.6 mmol) in

14445 anhydrous DMF (30 mL) was added a solution of 4-bromomethyl-2-(2-methylphenyl)benzoic acid methyl ester (6.00 g, 18.8 mmol), prepared as in Example 1178A-D, in anhydrous DMF (10 mL). Reaction stirred overnight at room temperature. Reaction diluted with EtOAc and washed with water and brine. Organic layer dried with Na_2SO_4, filtered, and concentrated in vacuo.

14450



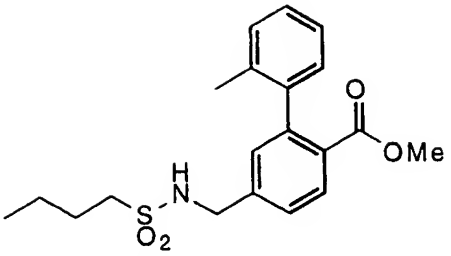
Example 1191B

4-Aminomethyl-2-(2-methylphenyl)benzoic acid methyl ester

To a flask at ambient temperature under N_2 containing 10% palladium on carbon

14455 catalyst (1.0 g) was added a solution of 4-azidomethyl-2-(2-methylphenyl)benzoic acid methyl ester (5.00 g, 17.8 mmol), prepared as inExample 1191A, in MeOH (75 mL). Two drops of conc. HCl added, and reaction stirred vigorously overnight under an atmosphere of H_2. Catalyst filtered off through celite and washed with MeOH. Filtrate concentrated in vacuo, and residue taken up in an aqueous 4N NaOH solution. Aqueous solution extracted

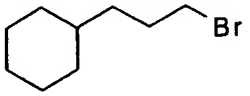
14460 with $CHCl_3$ (3x), and extracts dried with Na_2SO_4, filtered, and concentrated in vacuo to afford the desired product (1.37 g, 30%). m/e (DCI) 256 (MH^+)



Example 1191C

4-N-Butanesulfonylminomethyl-2-(2-methylphenyl)benzoic acid methyl ester

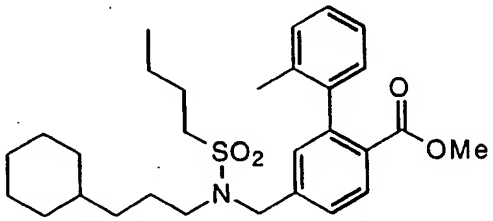
The desired compound was prepared using the method described in Example 1174A starting with 4-aminomethyl-2-(2-methylphenyl)benzoic acid methyl ester, prepared as in Example 1191B, and butanesulfonyl chloride. m/e (ESI) 374 (MH^-)



Example 1191D

1-Bromo-3-cyclohexylpropane

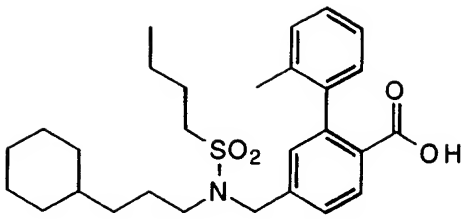
The desired compound was prepared according to the method of Example 1178D starting with 3-cyclohexyl-1-propanol. ^1H (300MHz, $CDCl_3$, δ) 3.40 (2H, t, J=8Hz), 1.85 (2H, m), 1.80-1.50 (6H, m), 1.40-1.10 (5H, m), 0.90 (2H, m).



Example 1191E

N-[4-N-(Butanesulfonyl)-N-(3-cyclohexylpropyl)aminomethyl-2-(2-methylphenyl)benzoic acid methyl ester

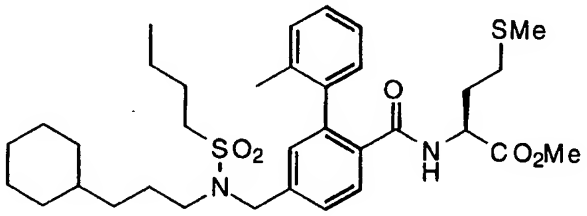
The desired compound was prepared using the method described in Example 1174B starting with the compounds from Example 1191C and Example 1191D. m/e (ESI) 500 (MH^+)



Example 1191F

N-[4-N-(Butanesulfonyl)-N-(3-cyclohexylpropyl)aminomethyl-2-(2-methylphenyl)benzoic acid

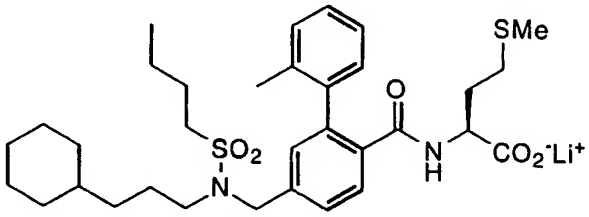
The acid was prepared using the method described in Example 403E starting with the compound from Example 1191E.



Example 1191G

N-[4-N-(Butanesulfonyl)-N-(3-cyclohexylpropyl)aminomethyl-2-(2-methylphenyl)benzoyl]methionine methyl ester

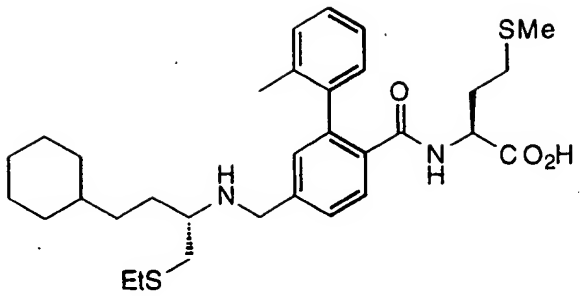
The compound was prepared using the method described inExample 403F starting with the compound fromExample 1191F. m/e (ESI) 629 (MH^-)



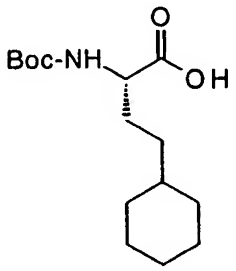
Example 1191H

N-[4-N-(Butanesulfonyl)-N-(3-cyclohexylpropyl)aminomethyl-2-(2-methylphenyl)benzoyl]methionine lithium salt

The desired compound was prepared according to the method ofExample 403I starting with the compound fromExample 1191G. ^1H (300MHz, DMSO-d6, δ) 7.54 (1H, d, J=8Hz), 7.41 (1H, bd, J=7Hz), 7.30-7.05 (5H, m), 6.97 (1H, d, J=7Hz), 4.42 (2H, s), 3.68 (1H, m), 3.10 (4H, bt, J=7Hz), 2.20-1.95 (5H, m), 1.91 (3H, s), 1.90-1.45 (9H, m), 1.45-1.20 (4H, m), 1.20-0.90 (6H, m), 0.88 (3H, t, J=8Hz), 0.73 (2H, m). m/e (ESI) 615 (MH^-) Anal.calc. for $C_{33}H_{47}LiN_2O_5S_2 \cdot 0.75\ H_2O$ C 62.29, H 7.68, N 4.40 Found C 62.18, H 7.75, N 4.36



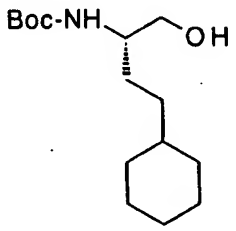
Example 1193



Example 1193A

(2S)-t-Butoxycarbonylamino-4-cyclohexylbutanoic acid

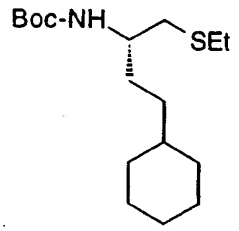
To a solution of Boc-homophenylalanine (3.00 g, 10.8 mmol) in CH_2Cl_2 at room temperature was added a solution of 4N HCl in dioxane (20 mL, 80 mmol), and mixture stirred overnight. Solvents concentrated, and white powder that resulted was reduced under high pressure (4 atm. H_2) using platinum/HCl. The white solid that resulted from the reduction was mixed with aqueous 4N NaOH (30 mL), water (30 mL), and THF (50 mL) at room temperature, and to this was added di-t-butyl dicarbonate (3.5 g, 16 mmol). Reaction heated at 70°C overnight. Reaction cooled to 0°C, and an aqueous solution of 3N HCl added until the pH reached 6. Product extracted out with $CHCl_3$, and extracts dried with Na_2SO_4, filtered, and concentrated in vacuo to produce a white solid (3.24 g, 106%). m/e (DCI) 286 (MH^+)



Example 1193B

(2S)-t-Butoxycarbonylamino-4-cyclohexylbutan-1-ol

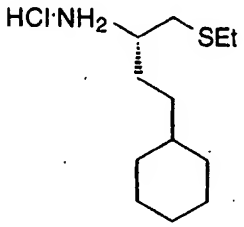
To a solution at -5°C under N_2 of (2S)-t-butoxycarbonylamino-4-cyclohexylbutanoic acid (3.24 g, 10.8 mmol), prepared as in Example 1193A, in anhydrous THF (20 mL) was added dropwise a 1.0M borane-THF complex (32.3 mL, 32.3 mmol) in THF. After addition, reaction stirred overnight at room temperature. Reaction cooled to 0°C and quenched with an aqueous 4N NaOH solution. Stirred 30 minutes at room temperature, and then, extracted with CH_2Cl_2 (3x). Extracts dried with Na_2SO_4, filtered, and concentrated in vacuo. Residue purified by flash chromatography on silica gel eluting with 30% EtOAc/Hexanes to afford the desired product as a colorless oil (696 mg, 23%). m/e (DCI) 272 (MH^+)



Example 1193C

(2S)-t-Butoxycarbonylamino-4-cyclohexyl-1-ethylthiobutane

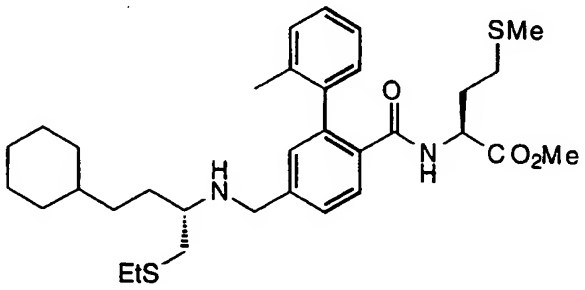
The desired compound was prepared using the method described in Example 403B and 403C starting with the product from Example 1193B. m/e (DCI) 316 (MH^+)



Example 1193D

(2S)-Amino-4-cyclohexyl-1-ethylthiobutane hydrochloride salt

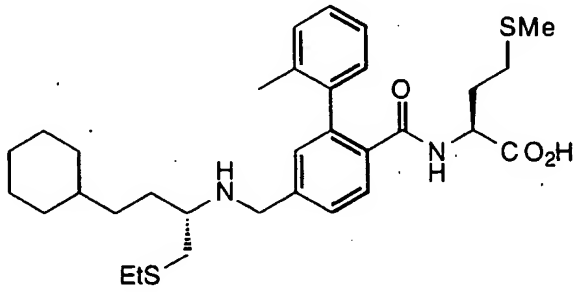
The desired compound was prepared using the method described in Example 403D starting with the product from Example 1193C.



Example 1193E

N-[4-N-(4-Cyclohexyl-1-ethylthiobutan-2-yl)aminomethyl-2-(2-methylphenyl)benzoyl]methionine methyl ester

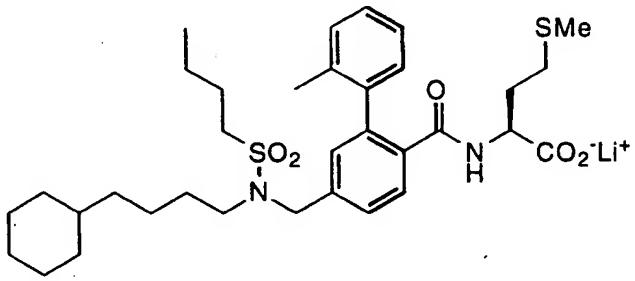
The desired compound was prepared using the method described in Example 403H starting with the product from Example 1193D and N-[4-formyl-2-(2-methylphenyl)benzoyl]methionine methyl ester, prepared as in Example 403G. m/e (ESI) 585 (MH^+)



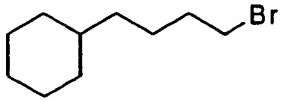
Example 1193F

N-[4-N-(4-Cyclohexyl-1-ethylthiobutan-2-yl)aminomethyl-2-(2-methylphenyl)benzoyl]methionine

The desired compound was prepared according to the method of Example 403I starting with the compound from Example 1193E. ^1H (300MHz, $CDCl_3$, δ) 7.72 (1H, m), 7.45 (1H, m), 7.40-7.00 (5H, m), 6.18 (1H, m), 4.36 (1H, m), 4.00 (2H, m), 2.95 (1H, m), 2.82 (1H, m), 2.73 (1H, m), 2.44 (2H, m), 2.20-2.00 (7H, m), 1.98 (3H, bs), 1.90-1.40 (7H, m), 1.20 (9H, t, J=8Hz), 0.87 (3H, m). m/e (ESI) 569 (MH^-) Anal.calc. for $C_{32}H_{46}N_2O_3S_2 \cdot 0.75\ H_2O$ C 65.77, H 8.19, N 4.79 Found C 65.74, H 8.08, N 4.69



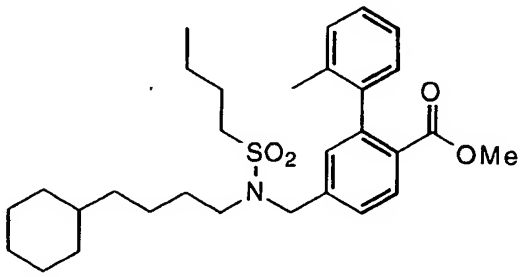
Example 1194



Example 1194A

1-Bromo-4-cyclohexylbutane

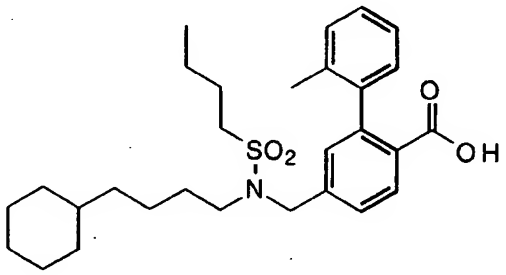
The desired compound was prepared according to the method of Example 1178D starting with 4-cyclohexyl-1-butanol. ^1H (300MHz, $CDCl_3$, δ) 3.40 (2H, t, J=8Hz), 1.83 (2H, m), 1.80-1.50 (6H, m), 1.42 (2H, m), 1.30-1.10 (5H, m), 0.85 (2H, m).



Example 1194B

4-N-(Butanesulfonyl)-N-(4-cyclohexylbutyl)aminomethyl-2-(2-methylphenyl)benzoic acid methyl ester

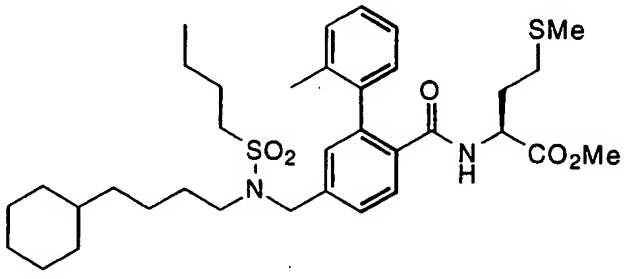
The desired compound was prepared using the method described in Example 1174B starting with the compounds from Example 1191C and Example 1194A. m/e (ESI) 514 (MH^+)



Example 1194C

4-N-(Butanesulfonyl)-N-(4-cyclohexylbutyl)aminomethyl-2-(2-methylphenyl)benzoic acid

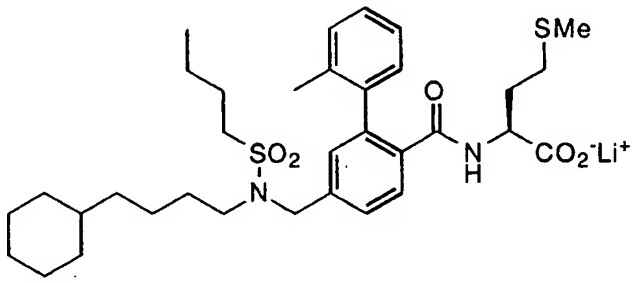
The acid was prepared using the method described in Example 403E starting with the compound from Example 1194B.



Example 1194D

N-[4-N-(Butanesulfonyl)-N-(4-cyclohexylbutyl)aminomethyl-2-(2-methylphenyl)benzoyl]methionine methyl ester

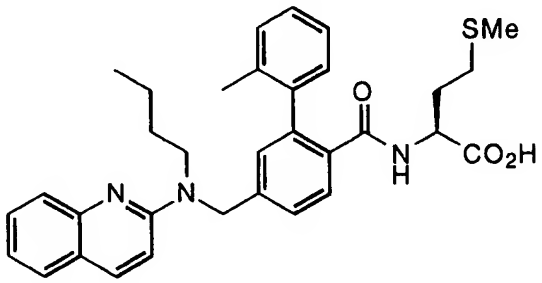
The compound was prepared using the method described in Example 403F starting with the compound from Example 1194C. ^{1}H (300MHz, $CDCl_3$, δ) 7.96 (1H, m), 7.43 (1H, dd, J=7&2Hz), 7.40-7.10 (5H, m), 5.90 (1H, bd, J=7Hz), 4.62 (1H, m), 4.44 (2H, s),3.64 (3H, s), 3.18 (2H, m), 2.96 (2H, m), 2.20-1.85 (8H, m), 1.75-1.50 (9H, m), 1.50-1.30 (4H, m), 1.25-1.00 (8H, m), 0.94 (3H, t, J=8Hz), 0.82 (2H, m).



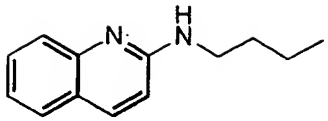
Example 1194E

N-[4-N-(Butanesulfonyl)-N-(4-cyclohexylbutyl)aminomethyl-2-(2-methylphenyl)benzoyl]methionine lithium salt

The desired compound was prepared according to the method ofExample 403I starting with the compound fromExample 1194D. ^{1}H (300MHz, DMSO-d6, δ) 7.56 (1H, d, J=8Hz), 7.41 (1H, dd, J=7&2Hz), 7.30-7.05 (5H, m), 6.98 (1H, d, J=7Hz), 4.42 (2H, bs), 3.68 (1H, m), 3.13 (4H, m), 2.20-1.95 (5H, m), 1.92 (3H, s), 1.90-1.45 (9H, m), 1.45-1.20 (4H, m), 1.20-0.90 (8H, m), 0.88 (3H, t, J=8Hz), 0.78 (2H, m). m/e (ESI) 629 (MH^-) Anal.calc. for $C_{34}H_{49}LiN_2O_5S_2 \cdot 0.75\ H_2O$ C 62.79, H 7.83, N 4.31 Found C 62.69, H 7.84, N 4.24



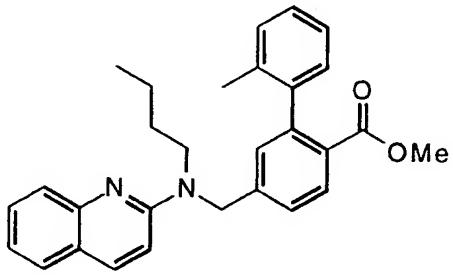
Example 1195



Example 1195A

N-Butyl-N-quinolin-2-ylamine

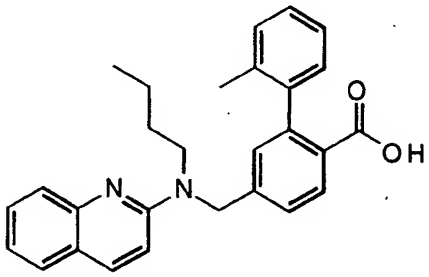
2-Chloroquinoline (500 mg, 3.06 mmol), butylamine (0.90 mL, 9.16 mmol), and diisopropylethylamine (0.82 mL, 4.58 mmol) were dissolved in acetonitrile (5 mL), and solution refluxed 2 days. Reaction cooled and diluted with EtOAc. Reaction washed with water and brine. Organic layer dried with Na_2SO_4, filtered, and concentrated in vacuo. Residue purified by flash chromatography on silica gel eluting with 15% EtOAc/Hexanes to afford the desired product as a pale yellow oil (188 mg, 31%). m/e (DCI) 201 (MH^+)



Example 1195B

4-N-Butyl-N-quinolin-2-ylaminomethyl-2-(2-methylphenyl)benzoic acid methyl ester

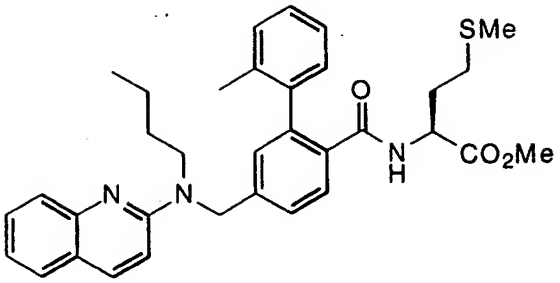
The desired compound was prepared according to the method of Example 1174B starting with 4-bromomethyl-2-(2-methylphenyl)benzoic acid methyl ester, prepared as in Example 1178A-D, and the compound from Example 1195A.



Example 1195C

4-N-Butyl-N-quinolin-2-ylaminomethyl-2-(2-methylphenyl)benzoic acid

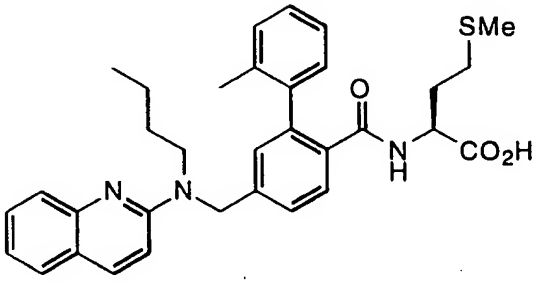
The desired acid was prepared using the method described in Example 403E starting with the product from Example 1195B.



Example 1195D

N-[4-N-Butyl-N-quinolin-2-ylaminomethyl-2-(2-methylphenyl)benzoyl]methionine methyl ester

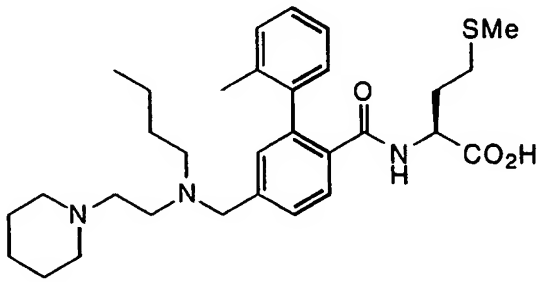
The desired compound was prepared using the method described in Example 403F starting with the product from Example 1195C. m/e (ESI) 570 (MH^+)



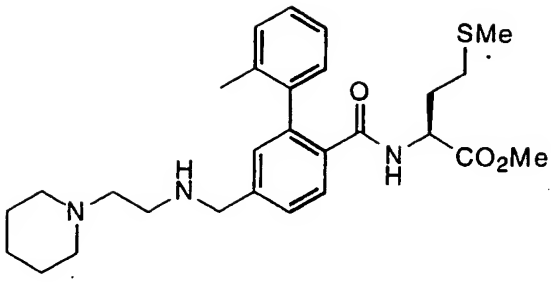
Example 1195E

N-[4-N-Butyl-N-quinolin-2-ylaminomethyl-2-(2-methylphenyl)benzoyl]methionine

The desired compound was prepared according to the method of Example 403I starting with the compound from Example 1195D. ^1H (300MHz, $CDCl_3$, δ) 7.95-7.80 (3H, m), 7.72 (1H, m), 7.60-7.40 (2H, m), 7.37 (1H, dd, J=7&2Hz), 7.30-7.00 (5H, m), 6.84 (1H, d, J=9Hz), 6.03 (1H, m), 5.03 (2H, bs), 4.44 (1H, m), 3.62 (2H, m), 2.20-2.00 (5H, m), 1.96 (3H, s), 1.85 (1H, m), 1.65 (2H, m), 1.51 (1H, m), 1.37 (2H, m), 0.93 (3H, t, J=8Hz). m/e (ESI) 554 (MH^-) Anal.calc. for $C_{33}H_{37}N_3O_3S \cdot 0.40\ H_2O$ C 70.41, H 6.77, N 7.46 Found C 70.62, H 6.68, N 7.07



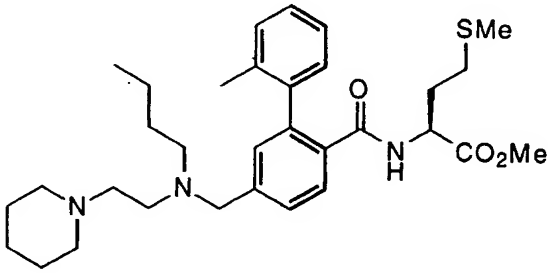
Example 1196



Example 1196A

N-[4-(N-(2-piperidin-1-ylethyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine methyl ester

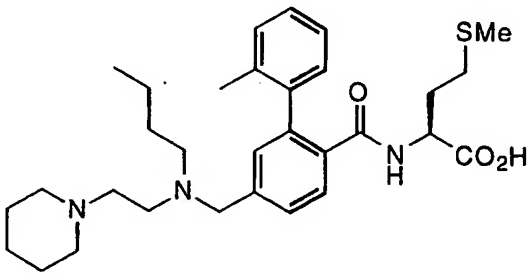
The desired compound was prepared using the method described in Example 403H starting with N-[4-formyl-2-(2-methylphenyl)benzoyl]methionine methyl ester, prepared as in Example 403G, and 1-(2-aminoethyl)piperidine. m/e (ESI) 498 (MH^+)



Example 1196B

N-[4-(N-Butyl-N-(2-piperidin-1-ylethyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine methyl ester

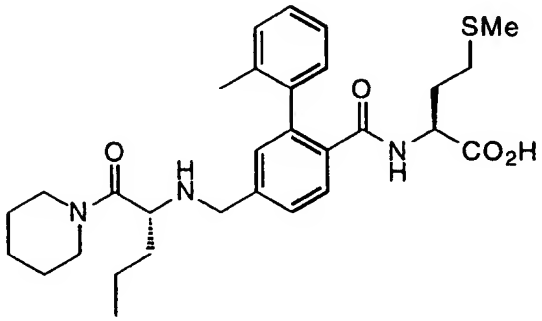
The desired compound was prepared using the method described in Example 403H starting with the compound prepared in Example 1196A and butyraldehyde. m/e (ESI) 552 (MH^-)



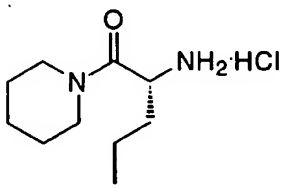
Example 1196C

N-[4-(N-Butyl-N-(2-piperidin-1-ylethyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine

The desired compound was prepared according to the method ofExample 403I starting with the compound fromExample 1196B. ^1H (300MHz, $CDCl_3$, δ) 7.62 (1H, d, J=8Hz), 7.30-7.10 (5H, m), 7.09 (1H, bs), 6.42 (1H, m), 4.35 (1H, m), 3.63 (2H, m), 3.05-2.75 (8H, m), 2.42 (2H, bt, J=7Hz), 2.20-1.90 (9H, m), 1.90-1.60 (5H, m), 1.55 (2H, m), 1.40 (2H, m), 1.22 (2H, m), 0.83 (3H, t, J=8Hz). m/e (ESI) 538 (MH^+) Anal.calc. for $C_{31}H_{45}N_3O_3S \cdot 0.75\ H_2O$ C 67.30, H 8.47, N 7.59 Found C 67.21, H 8.39, N 7.52



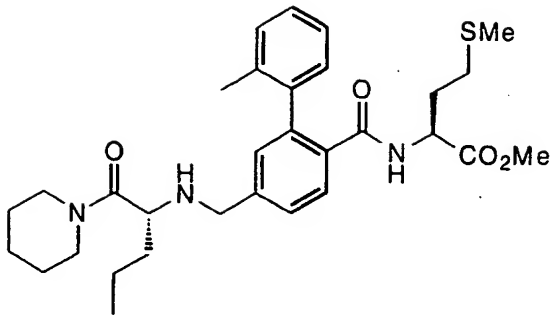
Example 1197



Example 1197A

N-(1-Morpholinocarbonyl)butylamine hydrochloride salt

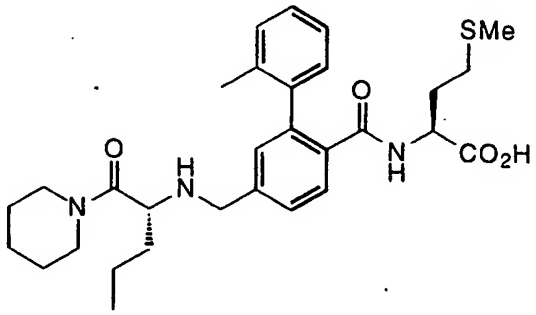
To a stirred solution at room temperature of Boc-L-norvaline (500 mg, 2.30 mmol) and piperidine (0.27 mL, 2.76 mmol) in DMF (5 mL) was added 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide (530 mg, 2.76 mmol). Reaction stirred overnight at room temperature. Reaction diluted with EtOAc and washed with water and brine. Organic layer dried with Na_2SO_4, filtered, and concentrated in vacuo. Residue mixed with a 4N HCl solution (10 mL, 40 mmol) in dioxane at room temperature overnight. Solvents concentrated in vacuo to afford the desired compound (222 mg, 44%). m/e (DCI) 185 (MH^+)



Example 1197B

N-[4-N-((1-Morpholinocarbonyl)butyl)aminomethyl-2-(2-methylphenyl)benzoyl]methionine methyl ester

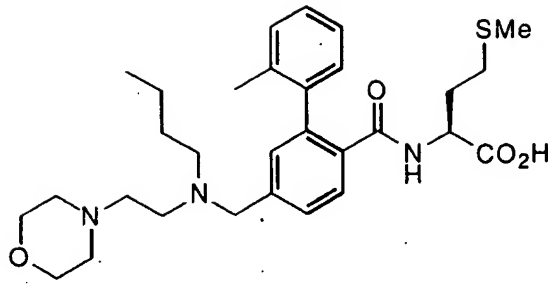
The desired compound was prepared using the method described in Example 403H starting with N-[4-formyl-2-(2-methylphenyl)benzoyl]methionine methyl ester, prepared as in Example 403G, and the compound prepared in Example 1197A. m/e (ESI) 554 (MH^+)



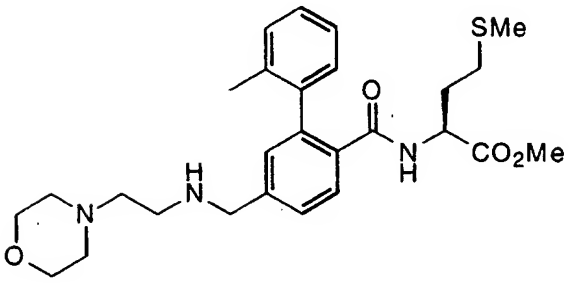
Example 1197C

N-[4-N-((1-Morpholinocarbonyl)butyl)aminomethyl-2-(2-methylphenyl)benzoyl]methionine

The desired compound was prepared using the method described in Example 403I starting with the compound from Example 1197B. ^1H (300MHz, $CDCl_3$, δ) 7.82 (1H, m), 7.43 (1H, dd, J=7&2Hz), 7.40-7.20 (4H, m), 7.17 (1H, d, J=2Hz), 6.08 (1H, m), 5.97 (1H, m), 4.43 (1H, m), 4.20-3.80 (2H, m), 3.69 (2H, m), 3.60-3.30 (3H, m), 2.20-1.90 (8H, m), 1.91 (2H, m), 1.66 (4H, m), 1.57 (4H, m), 1.30 (2H, m), 0.89 (3H, t, J=8Hz). m/e (ESI) 538 (MH^+) Anal.calc. for $C_{30}H_{41}N_3O_4S \cdot 0.75\ H_2O$ C 65.13, H 7.74, N 7.59 Found C 65.40, H 7.44, N 7.26



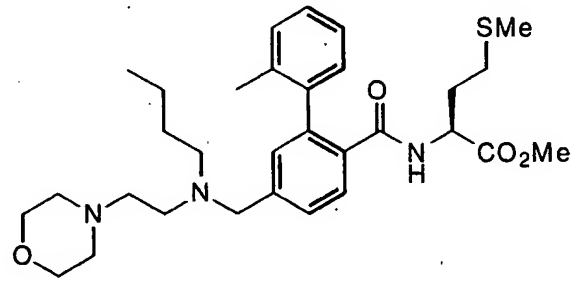
Example 1198



Example 1198A

N-[4-(N-(2-Morpholin-4-ylethyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine methyl ester

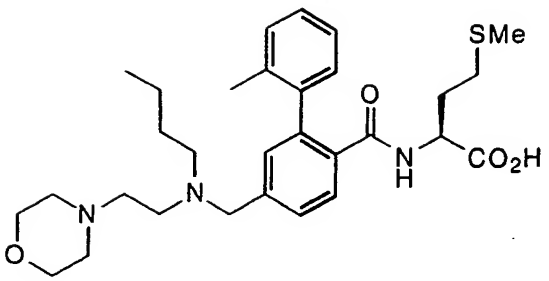
The desired compound was prepared using the method described in Example 403H starting with N-[4-formyl-2-(2-methylphenyl)benzoyl]methionine methyl ester, prepared as in Example 403G, and 4-(2-aminoethyl)morpholine. m/e (ESI) 500 (MH^+)



Example 1198B

N-[4-N-Butyl-N-(2-morpholin-4-ylethyl)aminomethyl-2-(2-methylphenyl)benzoyl]methionine methyl ester

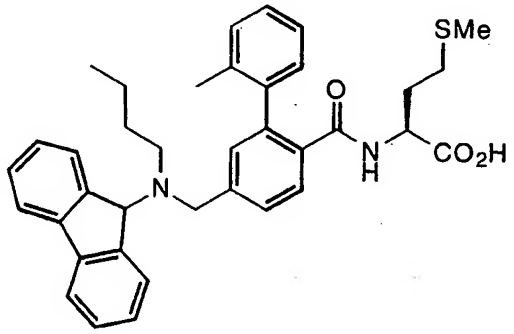
The desired compound was prepared using the method described in Example 403H starting with the compound prepared in Example 1198A and butyraldehyde. m/e (ESI) 554 (MH^-)



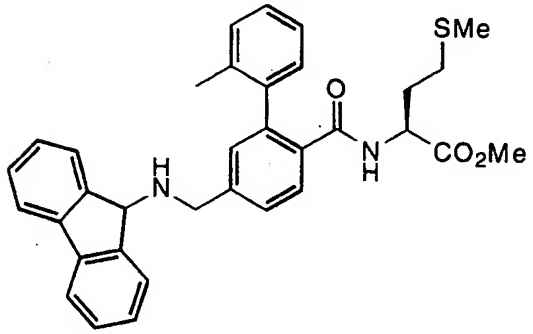
Example 1198C

N-[4-N-Butyl-N-(2-morpholin-4-ylethyl)aminomethyl-2-(2-methylphenyl)benzoyl]methionine

The desired compound was prepared according to the method of Example 403I starting with the compound from Example 1198B. ^{1}H (300MHz, $CDCl_3$, δ) 7.71 (1H, d, J=9Hz), 7.43 (1H, bd, J=8Hz), 7.30-7.10 (5H, m), 6.25 (1H, m), 4.39 (1H, m), 3.83 (2H, bs), 3.72 (4H, m), 2.89 (2H, m), 2.80-2.50 (8H, m), 2.20-1.80 (9H, m), 1.62 (1H, m), 1.50 (2H, m), 1.27 (2H, m), 0.88 (3H, t, J=8Hz). m/e (ESI) 540 (MH^+) Anal.calc. for $C_{30}H_{43}N_3O_4S \cdot 0.50\ H_2O$ C 65.42, H 8.05, N 7.63 Found C 65.22, H 7.92, N 7.47



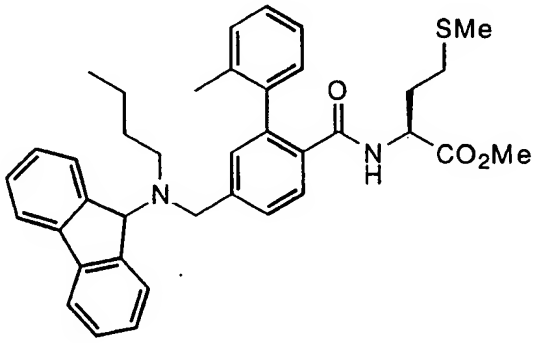
Example 1199



Example 1199A

N-[4-(N-(Fluoren-9-yl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine methyl ester

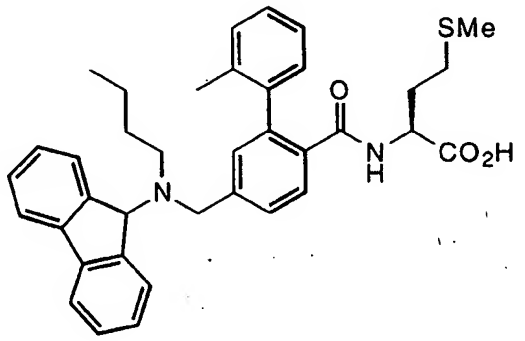
The desired compound was prepared using the method described inExample 403H starting with N-[4-formyl-2-(2-methylphenyl)benzoyl]methionine methyl ester, prepared as inExample 403G, and 9-aminofluorene hydrochloride salt m/e (ESI) 551 (MH^+)



Example 1199B

N-[4-N-Butyl-N-(fluoren-9-yl)aminomethyl-2-(2-methylphenyl)benzoyl]methionine methyl ester

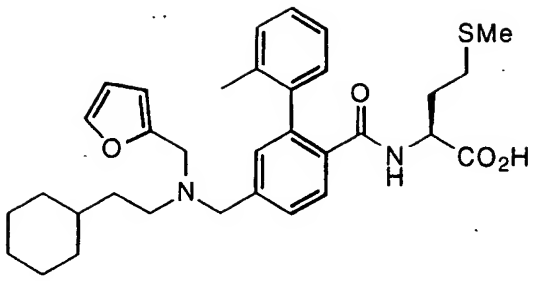
The desired compound was prepared using the method described inExample 403H starting with the compound prepared inExample 1199A and butyraldehyde. m/e (ESI) 605 (MH^-)



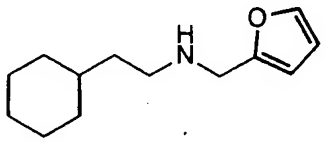
Example 1199C

N-[4-N-Butyl-N-(fluoren-9-yl)aminomethyl-2-(2-methylphenyl)benzoyl]methionine

The desired compound was prepared according to the method ofExample 403I starting with the compound fromExample 1199B. ^1H (300MHz, $CDCl_3$, δ) 7.91 (1H, m), 7.67 (3H, m), 7.47 (1H, bd, J=8Hz), 7.40-7.10 (10H, m), 5.84 (1H, m), 5.00 (1H, bs), 4.52 (1H, m), 3.53 (2H, bs), 2.64 (2H, m), 2.20-1.95 (8H, m), 1.90 (1H, m), 1.52 (3H, m), 1.32 (2H, m), 0.83 (3H, bt, J=8Hz). m/e (ESI) 591 (MH^-) Anal.calc. for $C_{37}H_{40}N_2O_3S \cdot 0.50\ H_2O$ C 73.85, H 6.87, N 4.65 Found C 74.07, H 6.70, N 4.63



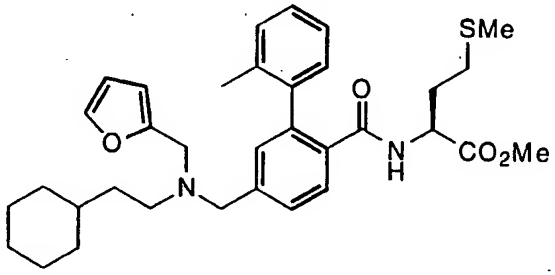
Example 1200



Example 1200A

N-(2-Cyclohexylethyl)-N-(furan-2-ylmethyl)amine

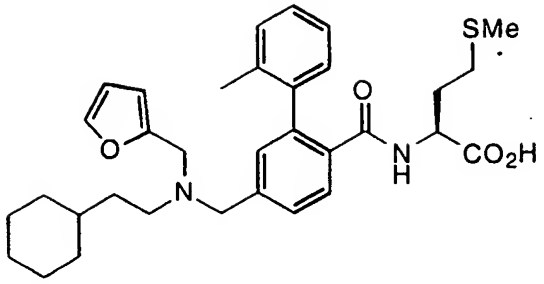
The desired amine was prepared using the method described in Example 1171A starting with cyclohexylethylamine and 2-furoic acid. m/e (DCI/NH_3) 208 (MH^+)



Example 1200B

N-[4-N-(2-Cyclohexylethyl)-N-(furan-2-ylmethyl)aminomethyl-2-(2-methylphenyl)benzoyl]methionine methyl ester

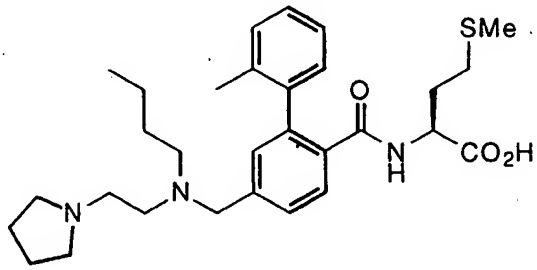
The desired compound was prepared using the method described in Example 403H starting with N-[4-formyl-2-(2-methylphenyl)benzoyl]methionine methyl ester, prepared as in Example 403G, and N-(2-Cyclohexylethyl)-N-(furan-2-ylmethyl)amine, prepared as in Example 1200A. m/e (ESI) 577 (MH^+)



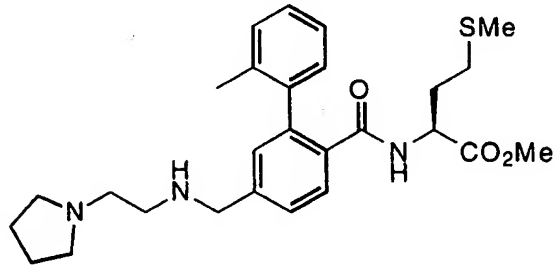
Example 1200C

N-[4-N-(2-Cyclohexylethyl)-N-(furan-2-ylmethyl)aminomethyl-2-(2-methylphenyl)benzoyl]methionine

The desired compound was prepared according to the method of Example 403I starting with the compound in Example 1200B. ^{1}H (300MHz, $CDCl_3$, δ) 7.81 (1H, d, J=8Hz), 7.56 (1H, m), 7.42 (1H, d, J=2Hz), 7.30-7.10 (5H, m), 6.37 (2H, bs), 6.15 (1H, d, J=8Hz), 4.45 (1H, m), 4.10-3.80 (4H, m), 2.67 (2H, m), 2.20-2.05 (5H, m), 2.00 (3H, s), 1.90 (1H, m), 1.80-1.40 (8H, m), 1.30-1.00 (4H, m), 0.88 (2H, m). m/e (ESI) 561 (MH^-) Anal.calc. for $C_{33}H_{42}N_2O_4S \cdot 1.00\ H_2O$ C 68.25, H 7.64, N 4.82 Found C 67.94, H 7.34, N 4.65



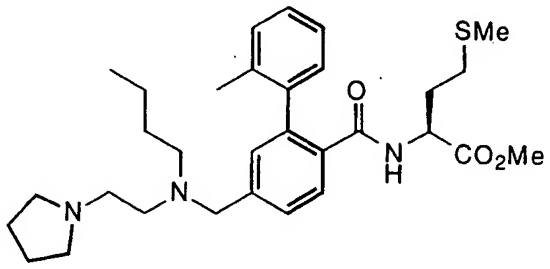
Example 1201



Example 1201A

N-[4-(N-(2-Pyrrolidin-1-ylethyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine methyl ester

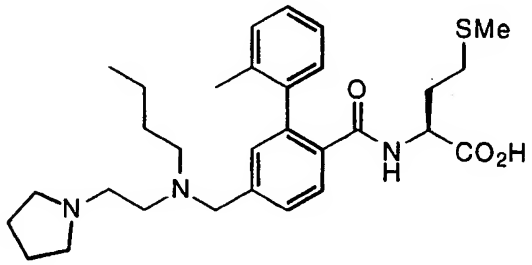
The desired compound was prepared using the method described in Example 403H starting with N-[4-formyl-2-(2-methylphenyl)benzoyl]methionine methyl ester, prepared as in Example 403G, and 1-(2-aminoethyl)pyrrolidine. m/e (ESI) 484 (MH^+)



Example 1201B

N-[4-N-Butyl-N-(2-pyrrolidin-1-ylethyl)aminomethyl-2-(2-methylphenyl)benzoyl]methionine methyl ester

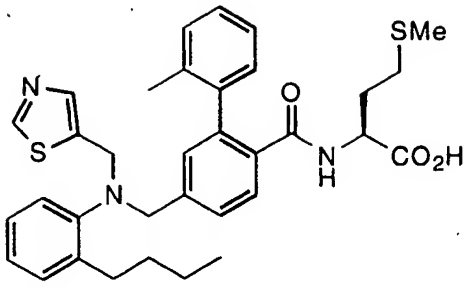
The desired compound was prepared using the method described in Example 403H starting with the compound prepared in Example 1201A and butyraldehyde. m/e (ESI) 540 (MH^+)



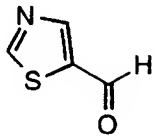
Example 1201C

N-[4-N-Butyl-N-(2-pyrrolidin-1-ylethyl)aminomethyl-2-(2-methylphenyl)benzoyl]methionine

The desired compound was prepared according to the method of Example 403I starting with the compound from Example 1201B. ^1H (300MHz, $CDCl_3$, δ) 7.66 (1H, d, J=8Hz), 7.35-7.10 (5H, m), 7.09 (1H, bs), 6.37 (1H, m), 4.36 (1H, m), 3.63 (2H, s), 3.16 (4H, m), 3.03 (2H, m), 2.84 (2H, m), 2.43 (2H, bt, J=8Hz), 2.20-1.80 (13H, m), 1.65 (1H, m), 1.41 (2H, m), 1.23 (2H, m), 0.85 (3H, t, J=8Hz). m/e (ESI) 524 (MH^+)
Anal.calc. for $C_{30}H_{43}N_3O_3S \cdot 1.00\ H_2O$ C 66.27, H 8.34, N 7.73 Found C 65.92, H 8.29, N 7.59



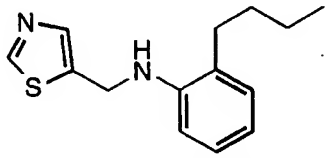
14860 Example 1202



Example 1202A

5-Thiazolecarboxaldehyde

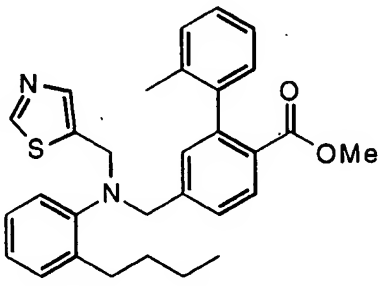
14865 The desired compound was prepared according to the method of Example 403G starting with 5-hydroxymethylthiazole. ^1H (300MHz, $CDCl_3$, δ) 10.13 (1H, s), 9.12 (1H, s), 8.54 (1H, s).



14870 Example 1202B

N-(2-Butylphenyl)-N-(thiazol-5-ylmethyl)amine

The desired compound was prepared according to the method ofExample 403H starting with 2-butylaniline and the aldehyde fromExample 1202A. m/e (DCI) 247 (MH^+)

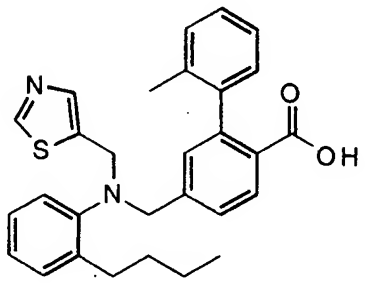


14875

Example 1202C

4-N-(2-Butylphenyl)-N-(thiazol-5-ylmethyl)aminomethyl-2-(2-methylphenyl)benzoic acid methyl ester

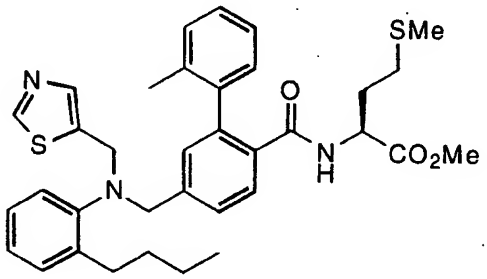
The desired compound was prepared according to the method of Example 1174B starting with 4-bromomethyl-2-(2-methylphenyl)benzoic acid methyl ester, prepared as in Example 1178A-D, and the compound from Example 1202B.



Example 1202D

4-N-(2-Butylphenyl)-N-(thiazol-5-ylmethyl)aminomethyl-2-(2-methylphenyl)benzoic acid

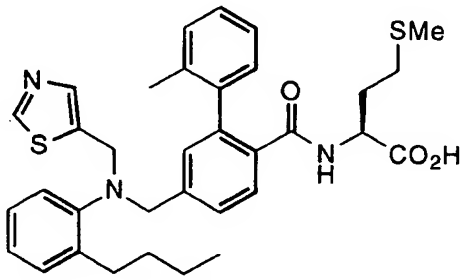
The desired acid was prepared using the method described in Example 403E starting with the product from Example 1202C.



Example 1202E

N-[4-N-(2-Butylphenyl)-N-(thiazol-5-ylmethyl)aminomethyl-2-(2-methylphenyl)benzoyl]methionine methyl ester

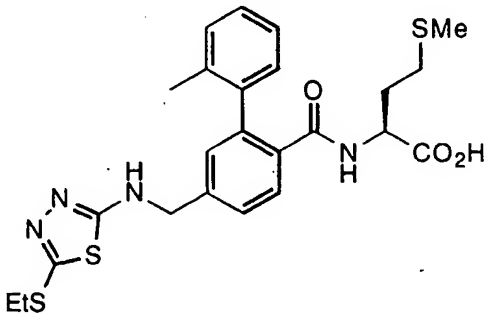
The desired compound was prepared using the method described inExample 403F starting with the product fromExample 1202D. m/e (ESI) 614 (MH^-)



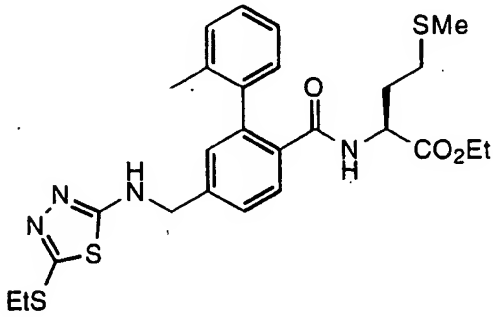
Example 1202F

N-[4-N-(2-Butylphenyl)-N-(thiazol-5-ylmethyl)aminomethyl-2-(2-methylphenyl)benzoyl]methionine

The desired compound was prepared according to the method ofExample 403I starting with the compound fromExample 1202E. ^{1}H (300MHz, $CDCl_3$, δ) 8.73 (1H, s), 7.91 (1H, bt, J=8Hz), 7.66 (1H, bs), 7.40-7.15 (5H, m), 7.15-6.90 (5H, bs), 5.88 (1H, d, J=8Hz), 4.57 (1H, m), 4.29 (2H, s), 4.13 (2H, s), 2.72 (2H, bt, J=8Hz), 2.20-1.80 (9H, m), 1.55 (3H, m), 1.35 (2H, m), 0.88 (3H, t, J=8Hz). m/e (ESI) 600 (MH^-)
Anal.calc. for $C_{34}H_{39}N_3O_3S_2$ C 67.86, H 6.53, N 6.98 Found C 67.57, H 6.43, N 6.71



Example 1203

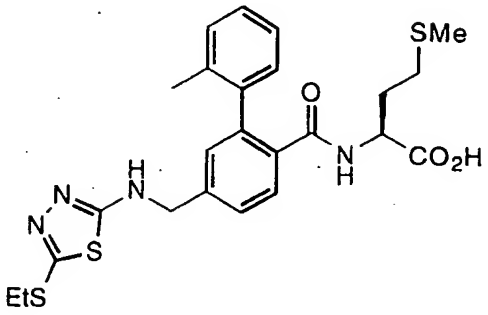


Example 1203A

N-[4-N-((2-Ethylthio)-1,3,4-thiadiazol-5-yl)aminomethyl-2-(2-methylphenyl)benzoyl]methionine ethyl ester

2-Amino-5-(ethylthio)-1,3,4-thiadiazole (419 mg, 2.60 mmol) and N-[4-formyl-2-(2-methylphenyl)benzoyl]methionine methyl ester (1.00 g, 2.60 mmol), prepared as inExample 403G, were mixed with toluene (4 mL) and refluxed under N_2 with a Dean-Stark trap overnight. Reaction diluted with EtOAc and washed with water and brine. Organic layer dried with Na_2SO_4, filtered, and concentrated in vacuo. To a solution of this residue in EtOH (8 mL) at 0°C under N_2 was added sodium borohydride (98 mg, 2.60 mmol), and mixture stirred vigorously at ambient temperature for 3 hours. Reaction diluted with EtOAc and washed with water and brine. Organic layer dried with Na_2SO_4, filtered, and concentrated in vacuo. Residue purified by flash chromatography on silica gel eluting

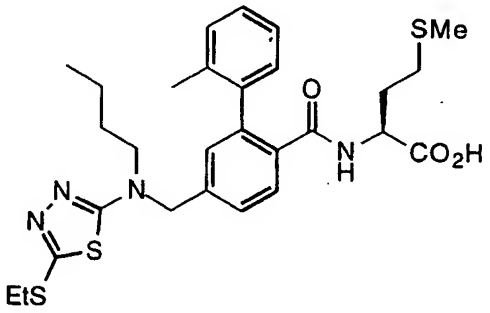
with 60% EtOAc/Hexanes to afford the desired product as a pale yellow oil (347 mg, 25%). m/e (ESI) 543 (MH^-)



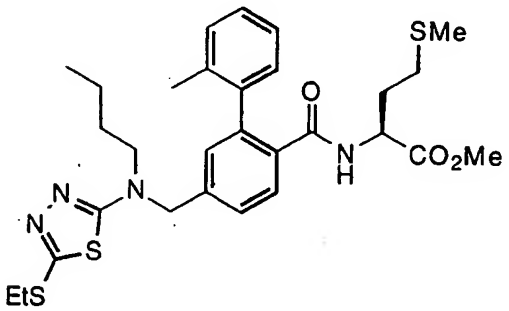
Example 1203B

N-[4-N-((2-Ethylthio)-1,3,4-thiadiazol-5-yl)aminomethyl-2-(2-methylphenyl)benzoyl]methionine

The desired compound was prepared according to the method ofExample 403I starting with the compound fromExample 1203A. ^1H (300MHz, $CDCl_3$, δ) 7.88 (1H, m), 7.46 (1H, m), 7.30-7.00 (5H, m), 5.94 (2H, m), 4.58 (1H, m), 4.42 (2H, bd, J=8Hz), 3.13 (2H, q, J=8Hz), 2.20-1.80 (9H, m), 1.67 (1H, m), 1.39 (3H, t, J=8Hz). m/e (ESI) 515 (MH^-) Anal.calc. for $C_{24}H_{28}N_4O_3S_3 \cdot 0.50\ H_2O$ C 54.83, H 5.56, N 10.66 Found C 54.86, H 5.41, N 11.04



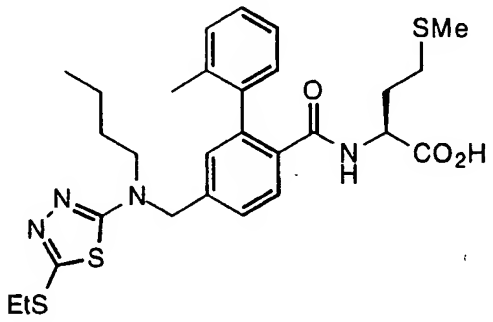
Example 1204



Example 1204A

N-[4-N-Butyl-N-((2-ethylthio)-1,3,4-thiadiazol-5-yl)aminomethyl-2-(2-methylphenyl)benzoyl]methionine methyl ester

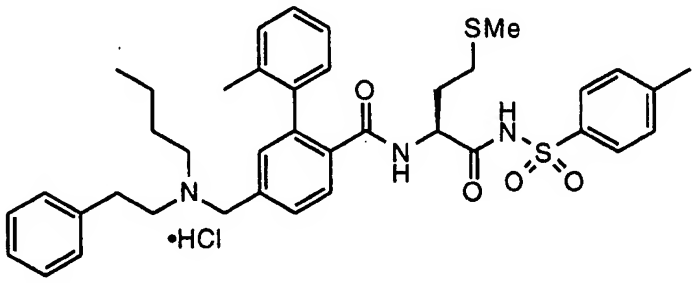
The desired compound was prepared using the method described in Example 403H starting with the compound prepared as in Example 1203A (methyl ester) and butyraldehyde. m/e (ESI) 587 (MH^+)



Example 1204B

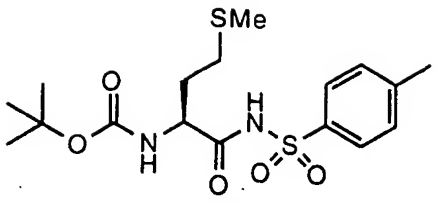
N-[4-N-Butyl-N-((2-ethylthio)-1,3,4-thiadiazol-5-yl)aminomethyl-2-(2-methylphenyl)benzoyl]methionine

The desired compound was prepared according to the method of Example 403I starting with the compound from Example 1204A. ^1H (300MHz, $CDCl_3$, δ) 7.81 (1H, m), 7.43 (1H, bd, J=8Hz), 7.30-7.10 (5H, m), 6.00 (1H, d, J=8Hz), 5.38 (2H, m), 4.48 (1H, m), 3.17 (2H, m), 3.02 (2H, q, J=8Hz), 2.20-1.80 (9H, m), 1.60 (3H, m), 1.32 (5H, t, J=8Hz), 0.88 (3H, t, J=8Hz). m/e (ESI) 571 (MH^-) Anal.calc. for $C_{28}H_{36}N_4O_3S_3 \cdot 0.50\ H_2O$ C 57.80, H 6.41, N 9.63 Found C 57.79, H 6.11, N 9.52



Example 1216

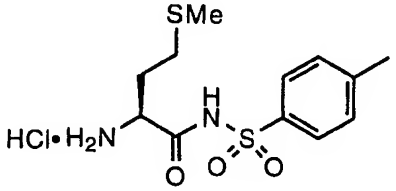
N-[4-(N-Butyl-N-(2-phenylethyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine p-tolylsulfonimide hydrochloride salt



Example 1216A

N-(tert-Butoxycarbonyl)-methionine p-tolylsulfonimide

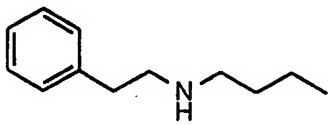
N-(tert-Butoxycarbonyl)-methionine (960 mg, 3.85 mmol) was dissolved in CH_2Cl_2 (50 mL), then added EDCI•HCl (1.12 g, 5.85 mmol), DMAP (287 mg, 2.35 mmol), and p-toluenesulfonamide (1.71 g, 10.0 mmol). The reaction was stirred at RT overnight, concentrated, dissolved in EtOAc (130 mL), then washed with water, 2N HCl, water, and brine. After drying over Na_2SO_4, filtration, and concentration, the compound was purified by chromatography using 1/1 hex/ EtOAc, then EtOAc. Recovered 635 mg (41%). MS (APCI) 403 $(M+H)^+$.



Example 1216B

Methionine p-tolylsulfonimide hydrochloride salt

The compound described in Example 1216A (610 mg, 1.52 mmol) was dissolved in 4N HCl in dioxane (10 mL), stirred at RT for 45 min., then diluted with Et_2O. The resultant solids were filtered off, and washed with Et_2O to give 465 mg (90%) white solids. MS (DCI/NH_3) 303 $(M+H)^+$.

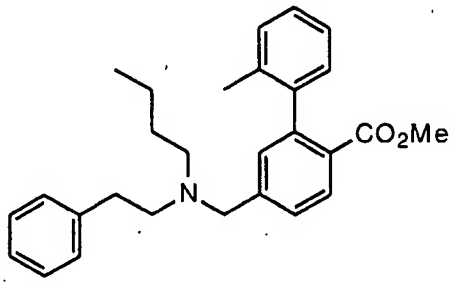


Example 1216C

N-Butyl-2-phenylethylamine

2-Phenethylamine (12.5 mL, 12.1 g, 99.5 mmol), butyraldehyde (13.2 mL, 10.8 g, 150 mmol), and 3Å molecular sieves were stirred at 50 °C for 1 h, then at RT for 5.5 h. The reaction was then diluted with CH_2Cl_2, filtered through celite, then concentrated to an oil. That oil was dissolved in absolute EtOH (150 mL-previously cooled to 0 °C), and $NaBH_4$ (5.7 g, 150 mmol) was added. The reaction was stirred at RT overnight, concentrated, partitioned between water and Et_2O, then the organic layer was washed with

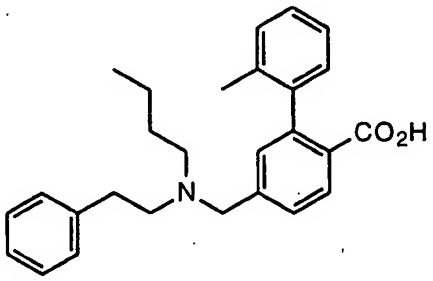
water and brine. After drying over Na_2SO_4, filtration, and concentration, the compound was purified by vacuum distillation using a 6" Vigeraux column (98-100 °C/ 9 mm). Recovered 8.2 g (46%). ^1H NMR ($CDCl_3$) δ 7.30 (m, 2H), 7.20 (m, 3H), 2.84 (m, 4H), 2.61 (dd, 2H), 1.43 (m, 2H), 1.32 (m, 2H), 1.08 (br s, 1H), 0.88 (t, 3H).



Example 1216D

4-(N-Butyl-N-(2-phenylethyl)aminomethyl)-2-(2-methylphenyl)benzoic acid methyl ester

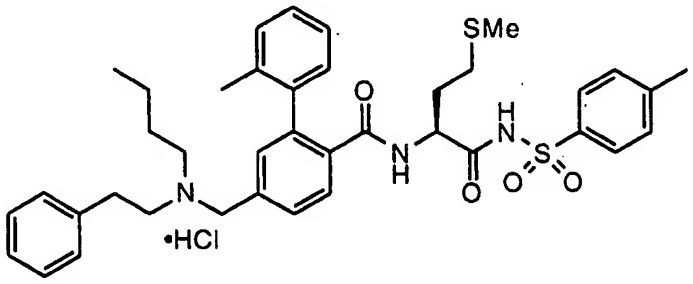
The title compound was prepared from the compound described in Example 1216C and the bromide described in Example 1178D using the method of Example 1178G. MS (APCI) 416 $(M+H)^+$.



Example 1216E

4-(N-Butyl-N-(2-phenylethyl)aminomethyl)-2-(2-methylphenyl)benzoic acid

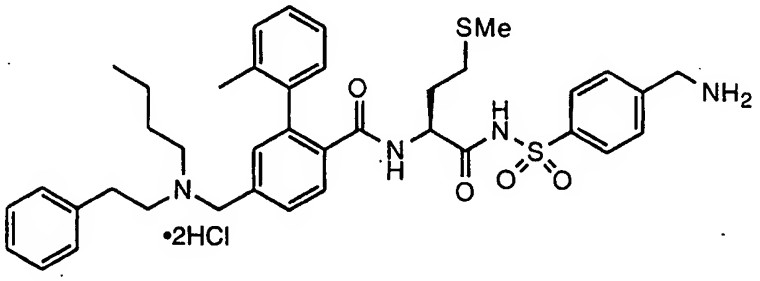
The title compound was prepared from the compound described in Example 1216D using the method of Example 1178H. MS (ESI) 402 $(M+H)^+$.



Example 1216F

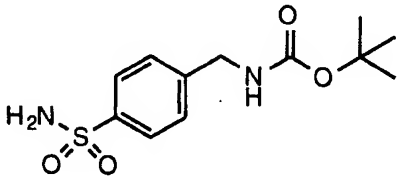
N-[4-(N-Butyl-N-(2-phenylethyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine p-tolylsulfonimide hydrochloride salt

The above compound was prepared according to the method of Example 1205D using the compounds described in Examples 1216B and 1216E, except the order of the aqueous work-up was saturated $NaHCO_3$, 2N HCl, brine, and the chromatography used 98/2/0.5 $CHCl_3/MeOH/CH_3CO_2H$. ^1H NMR ($CDCl_3$) δ 7.85 (m, 4H),7.26 (m, 12H), 6.47 (m, 1H), 4.60 (m, 1H), 4.30 (m, 2H), 3.20 (m, 6H), 2.43 (s, 3H), 2.08 (m, 3H), 1.90 (m, 7H), 1.83, 1.60 (both m, total 4H), 0.95 (m, 3H). MS (ESI) 684 $(M-H)^-$. Anal calcd for $C_{39}H_{48}ClN_3O_4S_2$: C, 64.84; H, 6.70; N, 5.82; Cl, 4.91. Found: C, 64.62; H, 6.82; N, 5.69; Cl, 4.62.



Example 1217

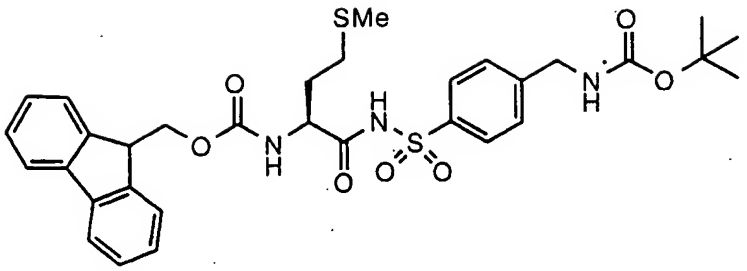
N-[4-(N-Butyl-N-(2-phenylethyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine 4-(aminomethyl)phenylsulfonimide dihydrochloride salt



Example 1217A

4-[(tert-Butoxycarbonyl)aminomethyl]phenylsulfonamide

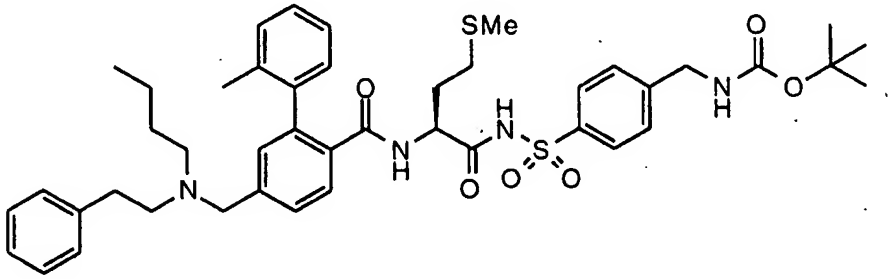
4-(Aminomethyl)phenylsulfonamide hydrochloride salt hemihydrate (1.0 g, 4.3 mmol) was dissolved in CH_2Cl_2 (20 mL), then triethylamine (0.66 mL, 0.48 g, 4.8 mmol) and di-tert-butyl-dicarbonate (0.95 g, 4.3 mmol) were added. The reaction was stiired at RT overnight, then concentrated and partitioned between water and EtOAc. The organic layer was washed with 2N HCl, saturated aqueous $NaHCO_3$ and brine, then dried over Na_2SO_4. After filtration and concentration recovered 1.3 g tacky white solids. MS (DCI/NH_3) 304 $(M+H+NH_3)^+$.



Example 1217B

N-(9-Fluorenylmethoxycarbonyl)-methionine 4-[(tert-butoxycarbonyl)aminomethyl] phenylsulfonimide

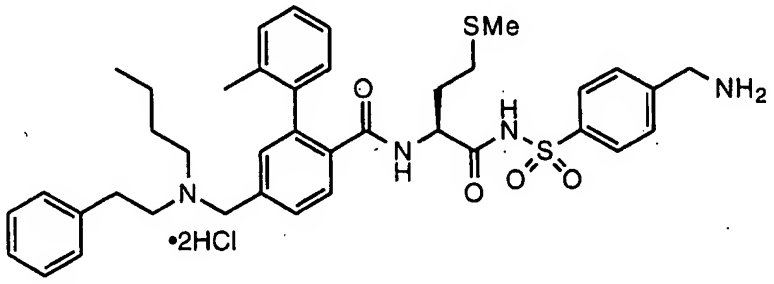
Using N-(9-Fluorenylmethoxycarbonyl)-methionine and the compound described in Example 1217A, the title compound was prepared by the method of Example 1216A. MS (ESI) 638 $(M-H)^-$.



Example 1217C

N-[4-(N-Butyl-N-(2-phenylethyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine 4-[(tert-butoxycarbonyl)aminomethyl]phenylsulfonimide

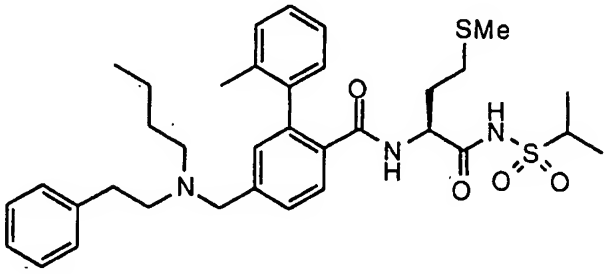
The compound described in Example 1217B was treated with piperidine in CH_2Cl_2 to give the free amine which was not purified, but directly reacted with the compound decribed in Example 1216E by the method of Example 1216F to give the title compound. MS (ESI) 801 $(M+H)^+$.



Example 1217D

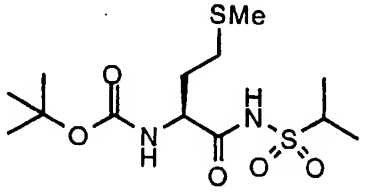
N-[4-(N-Butyl-N-(2-phenylethyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine 4-(aminomethyl)phenylsulfonimide dihydrochloride salt

Starting with the compound described in Example 1217C, the title compound was prepared by the method of Example 1216B. ^{1}H NMR (CD_3OD) δ 8.05 (d, 2H), 7.66 (m, 4H), 7.45 (br s, 1H), 7.25 (m, 10H), 4.53 (d, 2H), 4.25 (m, 1H), 4.24 (s, 2H), 3.33 (m, 2H), 3.24 (m, 2H), 3.10 (m, 2H), 2.10 (m, 5H), 1.97 (s, 3H), 1.80 (m, 3H), 1.60 (m, 1H), 1.40 (m, 2H), 0.98 (t, 3H). MS (ESI) 699 $(M-H)^-$. Anal calcd for $C_{39}H_{50}Cl_2N_4O_4S_2 \cdot 1.50\ H_2O$: C, 68.49; H, 6.67; N, 7.00. Found: C, 58.41; H, 6.61; N, 6.70.



Example 1218

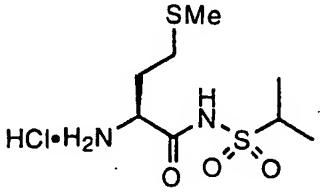
N-[4-(N-Butyl-N-(2-phenylethyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine isopropylsulfonimide



Example 1218A

N-(tert-Butoxycarbonyl)-methionine isopropylsulfonimide

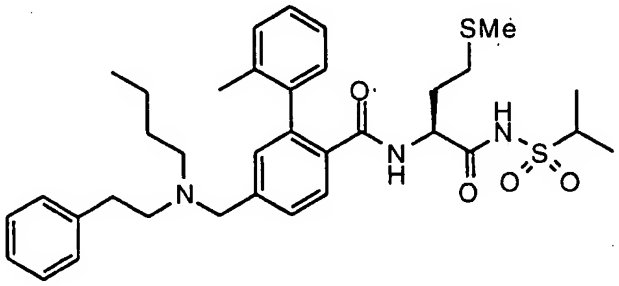
The title compound was prepared by the method of Example 1216A using isopropylsulfomamide. MS (DCI/NH_3) 372 $(M+H+NH_3)^+$.



Example 1218B

Methionine isopropylsulfonimide hydrochloride salt

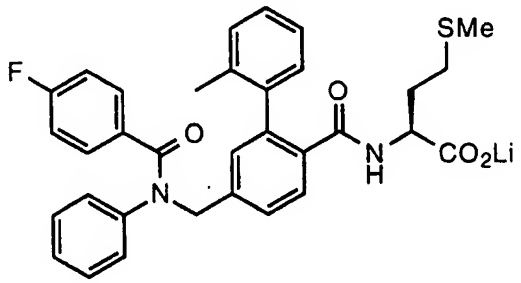
Starting with the compound described in Example 1218A,the title compound was prepared by the method of Example 1216B, except the product was isolated as a tan foam after strippng off the dioxane. MS (DCI/NH_3) 255 $(M+H)^+$.



Example 1218C

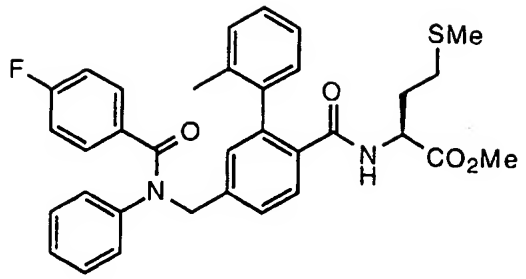
N-[4-(N-Butyl-N-(2-phenylethyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine isopropylsulfonimide

The above compound was prepared according to the method of Example 1205D using the compounds described in Examples 1218B and 1216E, except the order of the aqueous work-up was saturated $NaHCO_3$, 2N HCl, brine, and the chromatography used 98/2/0.5 $CHCl_3$/MeOH/CH_3CO_2H. ^1H NMR ($CDCl_3$) δ 7.91 (m, 1H), 7.43 (d, 1H), 7.32 (m, 3H), 7.18 (m, 7H), 5.83 (d, 1H), 4.43 (m, 1H), 3.77 (s, 2H), 3.65 (m, 1H), 2.80 (br s, 4H), 2.59 (m, 2H), 2.15, 2.02 (both m, total 8H), 1.82 (m, 1H), 1.50, 1.38, 1.28 (all m, total 11H), 0.86 (t, 3H). MS (ESI) 636 $(M-H)^-$. Anal calcd for $C_{35}H_{47}N_3O_4S_2$: C, 65.90; H, 7.43 N, 6.59. Found: C, 66.01; H, 7.36; N, 6.30.



Example 1227

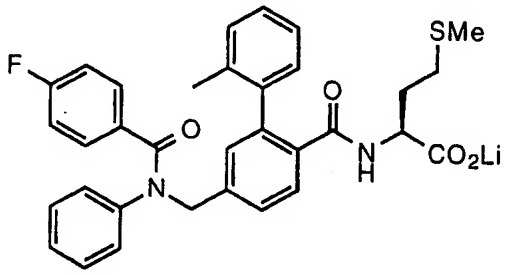
N-[4-N-(N-phenyl-N-(4-fluorobenzoyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine lithium salt.



Example 1227A

N-[4-N-(N-phenyl-N-(4-fluorobenzoyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine, methyl ester

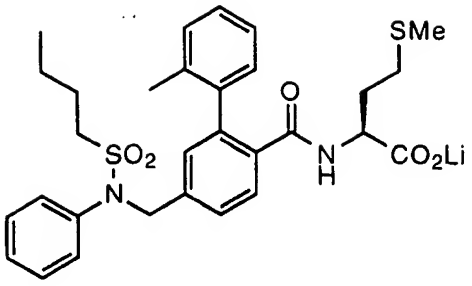
A mixture of 4-fluorobenzoyl chloride (0.053 g, 0.33 mmol), 1236C (0.103 g, 0.22 mmol), and 0.2 ml of pyridine in 5 ml of CH_2Cl_2 was stirred for 12 hours. The mixture was washed with 10% HCl and brine respectively, dried over $MgSO_4$. Flash chromatography of the residue eluting with 1:1 EtOAC/Hexane afforded 0.13 g of the title compound (99%). NMR($CDCl_3$) 7.84-7.94 (m, 1H); 7.38-7.48 (m, 1H); 7.05-7.38 (m, 10H); 5.85-5.92 (m, 1H); 5.10-5.27 (m, 2H); 4.56-4.67 (m, 1H); 3.62 (s, 3H); 1.95-2.20 (m, 8H); 1.7-2.0 (m, 1H); 1.5-1.7 (m, 1H). (DSI/NH3)/MS: 585$(M+H)^+$; 604 $(M+NH4)^+$.



Example 1227B

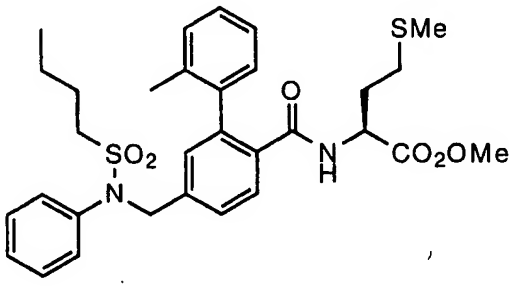
N-[4-N-(N-phenyl-N-(4-fluorobenzoyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine lithium salt.

Prepared according to the procedure of example 1178J from 1227A. NMR ^1H(MeOH-d4): 7.6-7.7 (1H, m); 7.3-7.5 (3H, m); 6.9-7.3 (14H, m); 5.18-5.38(2H, m); 4.1-4.22 (1H, m); 1.7-2.1 (10H, m). ESI(-)/MS: 569(M-Li).



Example 1228

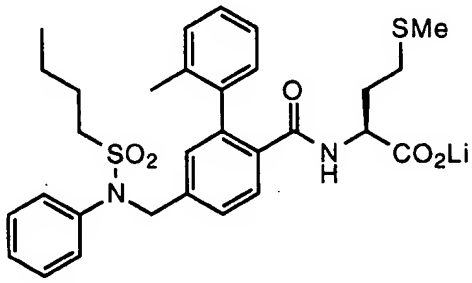
N-[4-N-(N-phenyl-N-(n-butanesulfonyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine lithium salt



Example 1228A

N-[4-N-(N-phenyl-N-(n-butanesulfonyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine, methyl ester

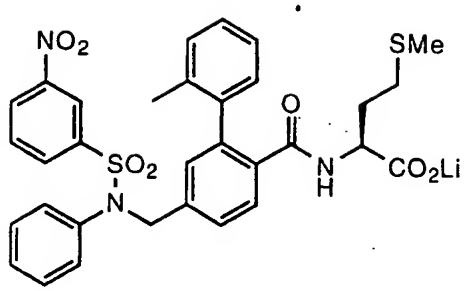
Prepared to the procedure of example 1229A from the reaction between 1236C and butanesulfonyl chloride. NMR($CDCl_3$) 7.80-7.90 (m, 1H); 7.12-7.38 (m, 10H); 7.05-7.11 (m, 1H); 5.8-5.9 (m, 1H); 4.78 (s, 2H); 4.5-4.65 (m, 1H); 3.62 (s, 3H); 3.0-3.08 (m, 2H); 1.5-2.15 (m, 14H); 0.92-0.98 (m, 3H). (DSI/NH_3)/MS: 583$(M+H)^+$; 600$(M+NH_4)^+$.



Example 1228B

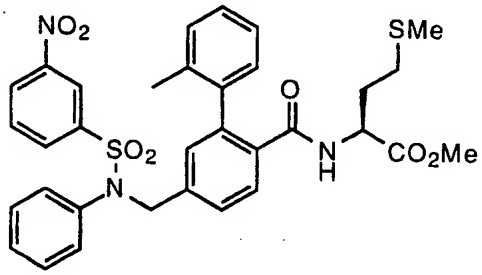
N-[4-N-(N-phenyl-N-(n-butanesulfonyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine lithium salt

Prepared according to the procedure of example 1178J from 1228A. NMR ^1H(MeOH-d4): 7.5-7.62 (1H, m); 7.1-7.4 (12H, m); 4.95 (2H, s); 4.1-4.22 (1H, m); 3.1-3.2 (2H, t); 1.7-2.1 (12H, m); 1.4-1.5 (2H, m); 0.9-1.0 (3H, t). ESI(-)/MS: 567(M-Li).



Example 1229

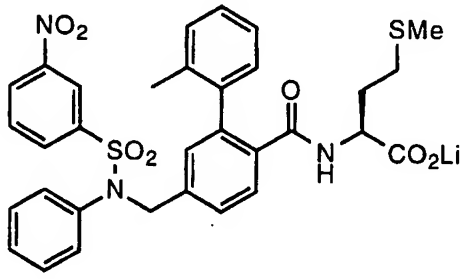
N-[4-N-(N-phenyl-N-(3-nitrobenzenesulfonyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine lithium salt



Example 1229A

N-[4-N-(N-phenyl-N-(3-nitrobenzenesulfonyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine, methyl ester

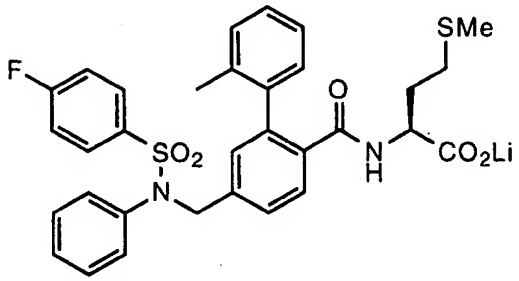
A mixture of 3-nitrophenylsulfonyl chloride (0.076 g, 0.34 mmol), 1236C (0.106 g, 0.23 mmol), and 0.2 ml of pyridine in 3 ml of CH_2Cl_2 was stirred for 12 hours. The mixture was washed with 10% HCl and brine respectively, dried over $MgSO_4$. Flash chromatography of the residue eluting with 1:1 EtOAC/Hexane afforded 0.12 g of the title compound (80%). NMR($CDCl_3$) 8.56 (m, 1H); 8.40-8.48 (m, 1H); 7.9-7.95 (m, 1H); 7.8-7.91 (m, 1H); 7.68-7.76 (m, 1H); 7.10-7.35 (m, 8H); 7.05 (m, 1H); 6.95-7.01 (m, 2H); 5.8-5.9 (m, 1H); 4.81 (s, 2H); 4.5-4.65 (m, 1H); 3.68 (s, 3H); 2.0-2.15 (m, 8H); 1.7-2.0 (m, 1H); 1.5-1.7 (m, 1H). (DSI/NH_3)/MS: 648$(M+H)^+$; 665$(M+NH_4)^+$.



Example 1229B

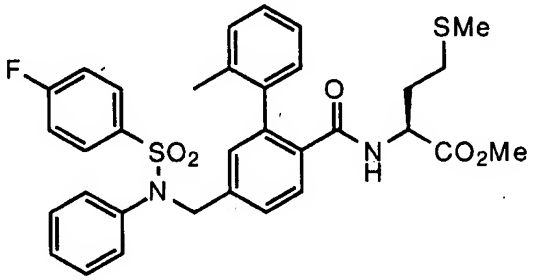
N-[4-N-(N-phenyl-N-(3-nitrobenzenesulfonyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine lithium salt

Prepared according to the procedure of example 1178J from 1229A. NMR ^{1}H(MeOH-d4): 8.35-8.45 (2H, m); 7.78-7.85 (2H, m), 7.5-7.6 (1H, m); 7.3-7.4 (1H, m); 7.1-7.3 (8H, m); 6.95-7.15 (3H, m); 4.9 (2H, s); 4.1-4.22 (1H, m); 1.7-2.1 (10H, m). ESI(-)/MS: 632(M-Li).



Example 1230

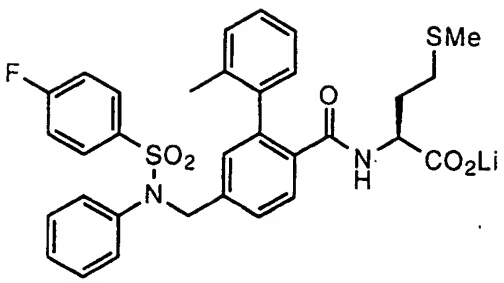
N-[4-N-(N-phenyl-N-(4-fluorobenzenesulfonyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine lithium salt



Example 1230A

N-[4-N-(N-phenyl-N-(4-fluorobenzenesulfonyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine, methyl ester

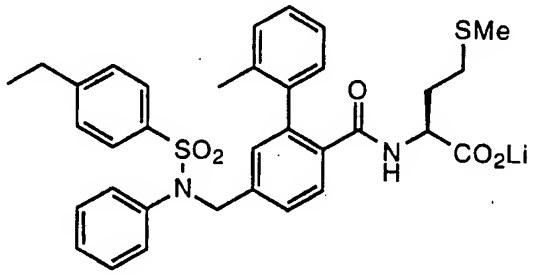
Prepared according to the procedure of example 1229A from reaction between 1236C and 4-fluorophenylsulfonyl chloride. NMR($CDCl_3$) 7.78-7.82 (m, 1H); 7.58-7.68 (m, 2H); 7.25-7.32 (m, 10H); 7.08 (m, 1H); 6.95-7.01 (m, 2H); 5.8-5.9 (m, 1H); 4.79 (s, 2H); 4.5-4.65 (m, 1H); 3.62 (s, 3H); 2.0-2.15 (m, 8H); 1.7-2.0 (m, 1H); 1.5-1.7 (m, 1H). (DSI/NH_3)/MS: 621$(M+NH_4)^+$; 638$(M+NH_4)^+$.



Example 1230B

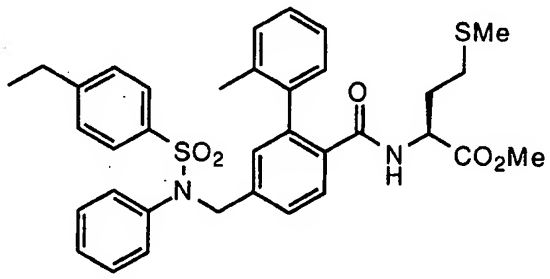
N-[4-N-(N-phenyl-N-(4-fluorobenzenesulfonyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine lithium salt

Prepared according to the procedure of example 1178J from 1230A. NMR ^{1}H(MeOH-d4): 7.65-7.8 (2H, m); 7.5-7.6 (1H, m); 7.1-7.3 (11H, m); 6.95-7.1 (3H, m); 4.9 (2H, s); 4.1-4.22 (1H, m); 1.7-2.1 (10H, m). ESI(-)/MS: 605(M-Li).



Example 1231

N-[4-N-(N-phenyl-N-(4-ethylbenzenesulfonyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine lithium salt

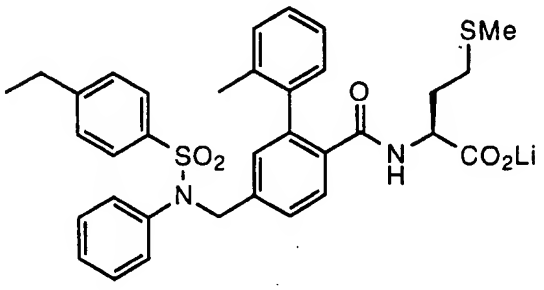


Example 1231A

N-[4-N-(N-phenyl-N-(4-ethylbenzenesulfonyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine, methyl ester

Prepared according to the procedure of example 1229A from reaction between 1236C and 4-ethylphenylsulfonyl chloride. NMR($CDCl_3$) 7.78-7.82 (m, 1H); 7.55-7.60 (m, 2H); 7.25-7.32 (m, 10H); 7.08 (m, 1H); 6.95-7.01 (m, 2H); 5.8-5.9 (m, 1H); 4.76 (s,

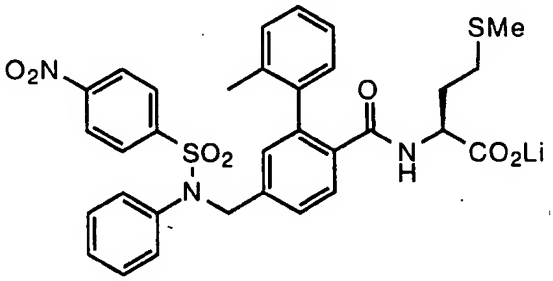
2H); 4.5-4.65 (m, 1H); 3.62 (s, 3H); 2.7-2.78(m, 2H); 2.0-2.15 (m, 8H); 1.7-2.0 (m, 1H); 1.5-1.7 (m, 1H); 1.2-1.35(m, 3H). (DSI/NH_3)/MS: 631$(M+H)^+$; 648$(M+NH_4)^+$.



Example 1231

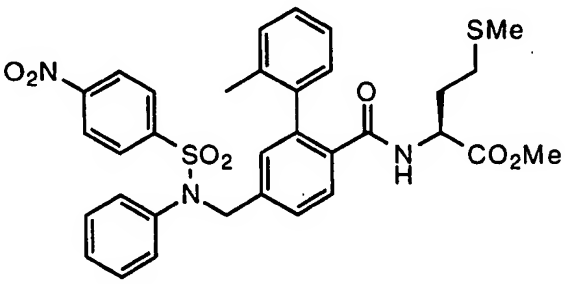
N-[4-N-(N-phenyl-N-(4-ethylbenzenesulfonyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine lithium salt

Prepared according to the procedure of example 1178J from 1231A. NMR ^1H(MeOH-d_4): 7.5-7.6 (3H, m); 7.1-7.4 (9H, m); 6.95-7.1 (3H, m); 4.9 (2H, s); 4.1-4.22 (1H, m); 2.7 (2H, q)1.7-2.1 (10H, m) (1H, m); 1.25 (3H, t). ESI(-)/MS: 615(M-Li).



Example 1232

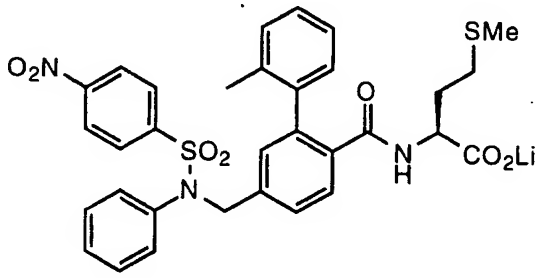
N-[4-N-(N-phenyl-N-(4-nitrobenzenesulfonyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine lithium salt



Example 1232A

N-[4-N-(N-phenyl-N-(4-nitrobenzenesulfonyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine, methyl ester

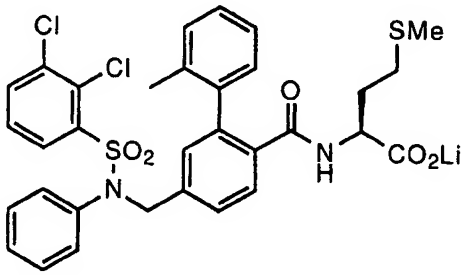
Prepared according to the procedure of example 1229A from reaction between 1236C and 4-nitrophenylsulfonyl chloride. NMR($CDCl_3$) 8.56 (m, 1H); 8.40-8.48 (m, 1H); 7.9-7.95 (m, 1H); 7.8-7.91 (m, 1H); 7.68-7.76 (m, 1H); 7.10-7.35 (m, 8H); 7.05 (m, 1H); 6.95-7.01 (m, 2H); 5.8-5.9 (m, 1H); 4.81 (s, 2H); 4.5-4.65 (m, 1H); 3.68 (s, 3H); 2.0-2.15 (m, 8H); 1.7-2.0 (m, 1H); 1.5-1.7 (m, 1H). (DSI/NH_3)/MS: 648$(M+H)^+$; 665$(M+NH_4)^+$.



Example 1232B

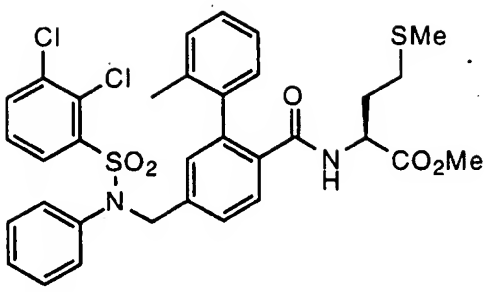
N-[4-N-(N-phenyl-N-(4-nitrobenzenesulfonyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine lithium salt

Prepared according to the procedure of example 1178J from 1232A. NMR ^1H(MeOH-d4): 8.45-8.55 (1H, m); 8.35-8.38 (1H, m); 8.0-8.1 (1H, m); 7.8-7.9 (1H, m); 7.5-7.7 (1H, m); 7.3-7.4 (1H, m); 7.1-7.3 (8H, m); 6.95-7.1 (3H, m); 4.9 (2H, s); 4.1-4.22 (1H, m); 1.7-2.1 (10H, m). ESI(-)/MS: 632(M-Li).



Example 1233

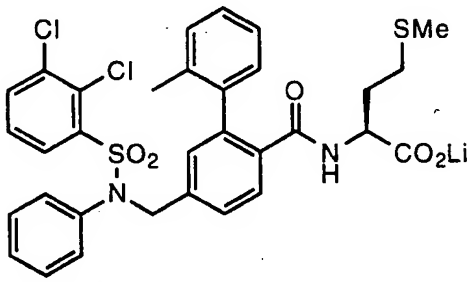
N-[4-N-(N-phenyl-N-(2,3-dichlorobenzenesulfonyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine lithium salt



Example 1233A

N-[4-N-(N-phenyl-N-(2,3-dichlorobenzenesulfonyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine, methyl ester

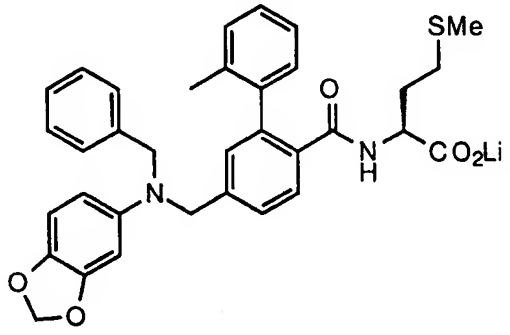
Prepared according to the procedure of example 1229A from reaction between 1236C and 3,4-dichlorophenylsulfonyl chloride. NMR($CDCl_3$) 7.6-7.7 (m, 1H); 7.5-7.55 (m, 1H); 7.55-7.6 (m, 1H); 7.40-7.43 (m, 1H); 7.15-7.36 (m, 8H); 7.08 (m, 1H); 6.95-7.01 (m, 2H); 5.8-5.9 (m, 1H); 4.78 (s, 2H); 4.5-4.65 (m, 1H); 3.62 (s, 3H); 2.0-2.15 (m, 8H); 1.7-2.0 (m, 1H); 1.5-1.7 (m, 1H). (DSI/NH_3)/MS: 671$(M+NH_4)^+$.



Example 1233B

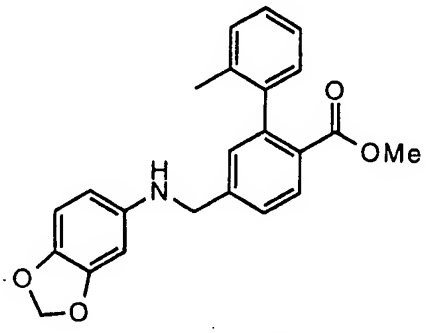
N-[4-N-(N-phenyl-N-(2,3-dichlorobenzenesulfonyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine lithium salt

Prepared according to the procedure of example 1178J from 1233A. NMR ^1H(MeOH-d4): 7.7-7.8 (2H, m); 7.5-7.6 (2H, m), 7.1-7.3 (9H, m); 6.95-7.1 (3H, m); 4.9 (2H, s); 4.1-4.22 (1H, m); 1.7-2.1 (10H, m). ESI(-)/MS: 655(M-Li).



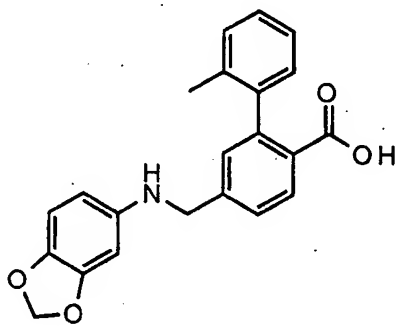
Example 1234

N-[4-N-(N-3,4-(methylenedioxy)phenyl-N-(4-fluorobenzyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine lithium salt.



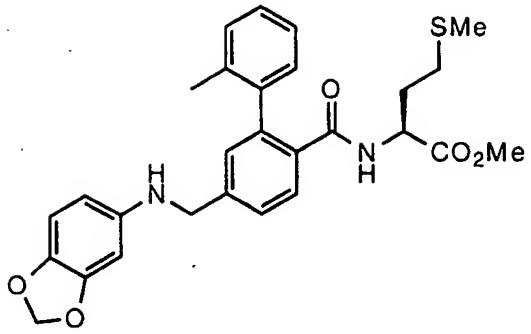
Example 1234A

Prepared according to the procedure of example 1236A. Instead of using aniline, 3,4-(methylenedioxy)aniline was used to make the title compound. NMR($CDCl_3$) 7.90-7.96 (m, 1H); 7.38-7.42 (m, 1H); 7.18-7.30 (m, 4H); 7.00-7.18 (m, 1H); 6.80-6.83 (m, 1H); 6.22-6.26 (m, 1H); 6.00-6.08 (m, 1H); 5.82 (s, m); 4.32-4.39 (m, 2H); 3.95-4.00 (m, 1H); 3.60 (s, 3H); 2.05 (s, 3H). (DSI/NH_3)/MS: 376$(M+H)^+$; 373$(M+NH_4)^+$.



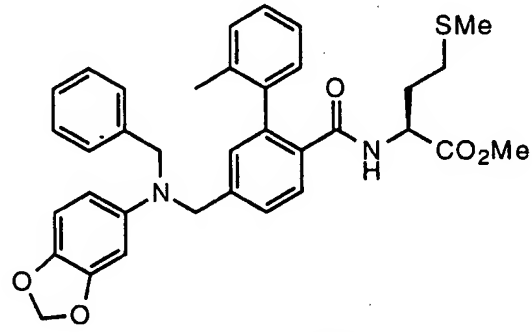
Example 1234B

Prepared according to the procedure of example 1178H from 1234A. NMR($CDCl_3$) 7.90-7.96 (m, 1H); 7.38-7.42 (m, 1H); 7.18-7.30 (m, 4H); 7.00-7.18 (m, 1H); 6.80-6.83 (m, 1H); 6.22-6.26 (m, 1H); 6.00-6.08 (m, 1H); 5.82 (s, 2H); 4.32-4.39 (m, 2H); 3.95-4.00 (m, 1H); 2.05 (s, 3H). (DSI/NH_3)/MS: 362$(M+H)^+$; 351$(M+NH_4)^+$.



Example 1234C

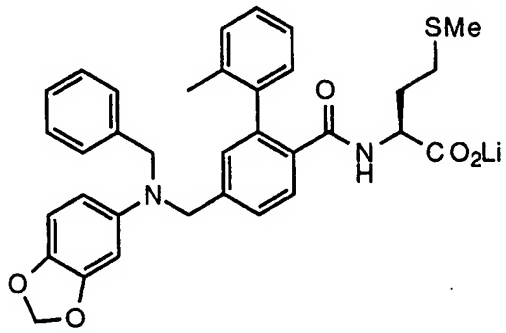
Prepared according to the procedure of example 1178I from 1234B. NMR($CDCl_3$) 7.85-7.95 (m, 1H); 7.18-7.30 (m, 6H); 7.00-7.18 (m, 1H); 6.6-6.65 (m, 1H); 6.35-6.40 (m, 1H); 6.10-6.20 (m, 1H); 5.82 (m, 3H); 4.5-4.70 (m, 3H); 3.61 (s, 3H); 2.0-2.15 (m, 8H); 1.7-2.0 (m, 1H); 1.5-1.7 (m, 1H). (DSI/NH_3)/MS: 507$(M+H)^+$; 324$(M+NH_4)^+$.



Example 1234D

N-[4-N-(N-(3,4-methylenedioxy)phenyl-N-(4-fluorobenzyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine, methyl ester

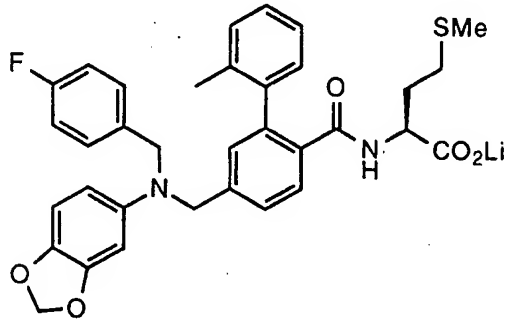
Prepared according to the procedure of example 1236A from reaction between 1235C and benzyl bromide. NMR($CDCl_3$) 7.85-7.95 (m, 1H); 7.18-7.30 (m, 10H); 7.02-7.18 (m, 1H); 6.6-6.65 (m, 1H); 6.35-6.40 (m, 1H); 6.15-6.20 (m, 1H); 5.82 (m, 3H); 4.59-4.70 (m, 3H); 4.57 (s, 2H); 3.62 (s, 3H); 2.0-2.15 (m, 8H); 1.7-2.0 (m, 1H); 1.5-1.7 (m, 1H). (DSI/NH_3)/MS: 597$(M+H)^+$.



Example 1234E

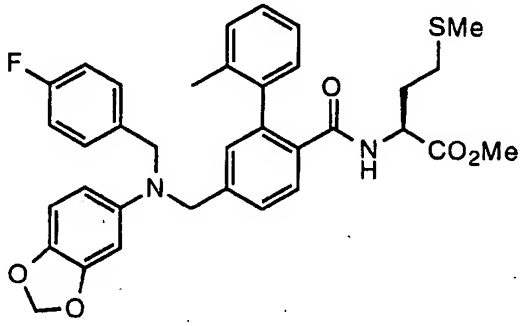
N-[4-N-(N-3,4-(methylenedioxy)phenyl-N-(4-fluorobenzyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine lithium salt.

Prepared according to the procedure of example 1178J from 1234D. NMR ^{1}H(MeOH-d4): 7.5-7.6 (1H, m); 7.2-7.25 (1H, m); 7.0-7.2 (9H, m); 6.9-7.0 (2H, m); 6.5-6.57 (1H, m); 6.3 (1H, m); 6.1 (1H, m); 5.75 (2H, s); 4.45 (2H, s); 4.4 (2H, s); 4.1-4.2 (1H, m); 1.7-2.1 (10H, m). ESI(-)/MS: 581(M-Li).



Example 1235

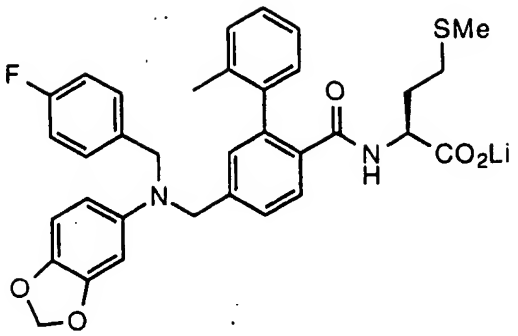
N-[4-N-(N-3,4-(methylenedioxy)phenyl-N-(4-fluorobenzyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine lithium salt



Example 1235A

N-[4-N-(N-3,4-(methylenedioxy)phenyl-N-(4-fluorobenzyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine, methyl ester

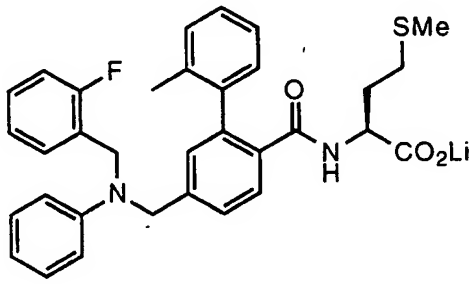
Prepared according to the procedure of example 1236A from reaction between 1234C and 4-fluorobenzyl bromide. NMR($CDCl_3$) 7.85-7.95 (m, 1H); 7.18-7.61 (m, 7H); 6.92-7.18 (m, 3H); 6.6-6.65 (m, 1H); 6.35-6.40 (m, 1H); 6.15-6.20 (m, 1H); 5.82 (m, 3H); 4.57-4.65 (m, 1H); 4.53 (s, 2H); 4.50 (s, 2H); 3.65 (s, 3H); 2.0-2.15 (m, 8H); 1.7-2.0 (m, 1H); 1.5-1.7 (m, 1H). (DSI/NH_3)/MS: 614$(M+H)^+$.



Example 1235B

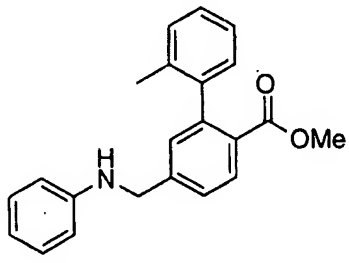
N-[4-N-(N-3,4-(methylenedioxy)phenyl-N-(4-fluorobenzyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine lithium salt

Prepared according to the procedure of example 1178J from 1235A. NMR ^{1}H(MeOH-d4): 7.5-7.6 (1H, m); 7.2-7.25 (1H, m); 7.0-7.2 (8H, m); 6.9-7.0 (2H, m); 6.5-6.57 (1H, m); 6.3 (1H, m); 6.1 (1H, m); 5.75 (2H, s); 4.45 (2H, s); 4.4 (2H, s); 4.1-4.2 (1H, m); 1.7-2.1 (10H, m). ESI(-)/MS: 599(M-Li).



Example 1236

N-[4-N-(N-phenyl-N-(2-fluorobenzyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine lithium salt

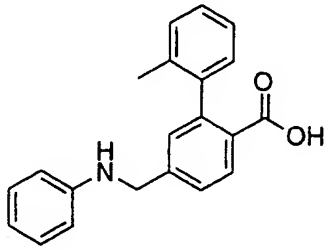


Example 1236A

4-(N-phenyl)aminomethyl-2-(2-methylphenyl)benzoic acid, methyl ester

A mixture of 4-Bromomethyl-2-(2-methylphenyl)benzoic acid, methyl ester (6.12 g, 20 mmol), aniline (1.68 g, 20 mmol), $NaHCO_3$ (1.68 g, 40 mmol), and $Bu_4N^+I^-$ (0.74g, 2

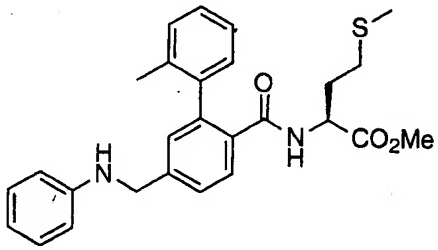
mmol) in 50 ml of DMF was heated at 75°C under N_2 for 12 hours. The reaction mixture was quenched by adding 400 ml of water. The solution was then extracted by 300 ml of EtOAc, washed by brine and dried over $MgSO_4$. Flash chromatography of residue on silica gel eluting with 80:20 EtOAc/Hexane afforded 6.1 g of pure product(96%). NMR($CDCl_3$) 7.85-7.95 (m, 1H); 7.40-7.45 (m, 1H); 7.0-7.36 (m, 7H); 6.68-6.78 (m, 1H); 6.58-6.65 (m, 2H); 4.2 (s, 2H); 4.05-4.2 (m, 1H); 3.58 (s, 3H); 2.05 (s, 3H). (DSI/NH_3)/MS: 332$(M+H)^+$, 349$(M+NH_4)^+$.



Example 1236B

4-(N-phenyl)aminomethyl-2-(2-methylphenyl)benzoic acid

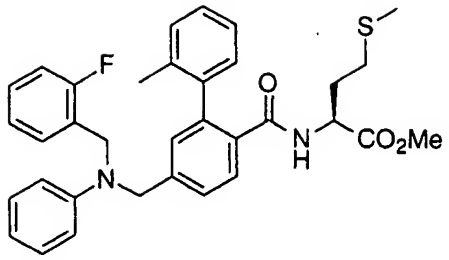
Prepared according to the procedure of example 1178H from 1236A. NMR($CDCl_3$) 7.85-7.95 (m, 1H); 7.40-7.45 (m, 1H); 7.0-7.36 (m, 7H); 6.68-6.78 (m, 1H); 6.58-6.65 (m, 2H); 4.2 (s, 2H); 4.05-4.2 (m, 1H); 2.05 (s, 3H). (DSI/NH_3)/MS: 318$(M+H)^+$, 335$(M+NH_4)^+$.



Example 1236C

N-4-[(N-phenyl)aminomethyl-2-(2-methylphenyl)benzoyl]methionine, methyl ester

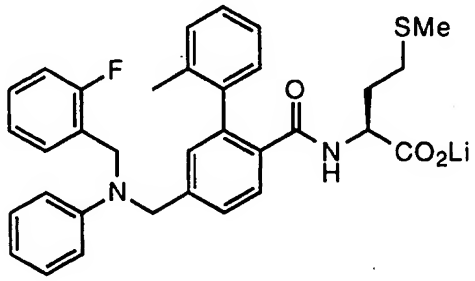
Prepared according to the procedure of example 1178I from 1236B. NMR($CDCl_3$) 7.85-7.95 (m, 1H); 7.41-7.47 (m, 1H); 7.1-7.36 (m, 7H); 6.68-6.78 (m, 1H); 6.58-6.65 (m, 2H); 5.85-5.95 (m, 1H); 4.56-4.68 (m, 1H); 4.2 (s, 2H); 4.05-4.2 (m, 1H); 3.62 (s, 3H); 2.05 (s, 3H); 2.0-2.15 (m, 8H), 1.7-2.0 (m, 1H), 1.5-1.7 (m, 1H).. (DSI/NH_3)/MS: 463$(M+H)^+$, 480$(M+NH_4)^+$.



Example 1236D

N-[4-N-(N-phenyl-N-(2-fluorobenzyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine, methyl ester

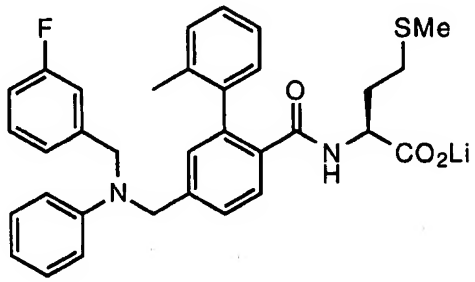
Prepared according to the procedure of 1236A from reaction between 1236C and 2-fluorobenzyl bromide. NMR($CDCl_3$) 7.85-7.95 (m, 1H); 7.0-7.4 (m, 12H); 6.65-6.78 (m, 3H); 5.8-5.9 (m, 1H); 4.75 (m, 4H); 4.58-4.65 (m, 1H); 3.65 (s, 3H), 2.0-2.15 (m, 8H); 1.7-2.0 (m, 1H); 1.5-1.7 (m, 1H). MS/(DSI/NH_3): 571$(M+H)^+$.



Example 1236E

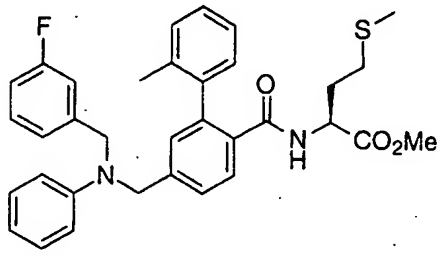
N-[4-N-(N-phenyl-N-(2-fluorobenzyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine lithium salt

Prepared according to the procedure of example 1178J for making lithium salt. NMR ^1H(MeOH-d_4): 7.6-7.7 (1H, d); 7.3-7.4 (1H, d); 7.0-7.4 (9H, m); 6.6-6.85 (6H, m); 4.7 (2H, s); 4.65 (2H, s); 4.2-4.3 (1H, m); 1.5-2.2 (10H, m). ESI(-)/MS: 555(M-Li).



Example 1237

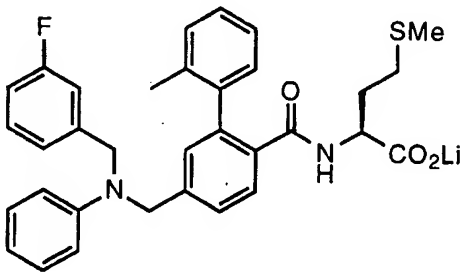
N-[4-N-(N-phenyl-N-(3-fluorobenzyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine lithium salt



Example 1237A

N-[4-N-(N-phenyl-N-(3-fluorobenzyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine, methyl ester

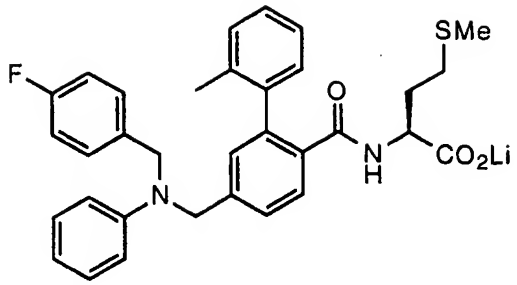
Prepared according to the procedure of 1236A from reaction between 1236C and 3-fluorobenzyl bromide. NMR($CDCl_3$) 7.85-7.95 (m, 1H); 6.9-7.4 (m, 12H); 6.75-6.8 (m, 3H); 5.8-5.9 (m, 1H); 4.70 (s, 2H); 4.58-4.65 (m, 3H); 3.62 (s, 3H); 2.0-2.15 (m, 8H), 1.7-2.0 (m, 1H); 1.5-1.7 (m, 1H). (DSI/NH_3)/MS: 571$(M+H)^+$.



Example 1237B

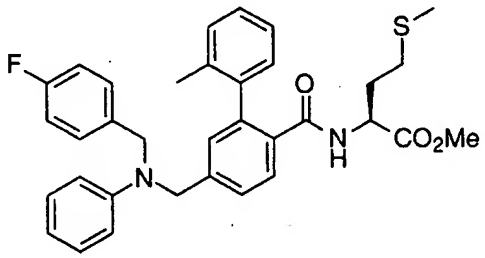
N-[4-N-(N-phenyl-N-(3-fluorobenzyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine lithium salt

Prepared according to the procedure of example 1178J from 1237A. NMR ^1H(MeOH-d4): 7.6-7.7 (2H, m); 6.86-7.4 (10H, m); 6.6-6.85 (4H, m); 4.75-4.85 (4H, m); 4.18-4.3 (1H, m); 1.6-2.2 (10H, m). ESI(-)/MS: 555(M-Li).



Example 1238

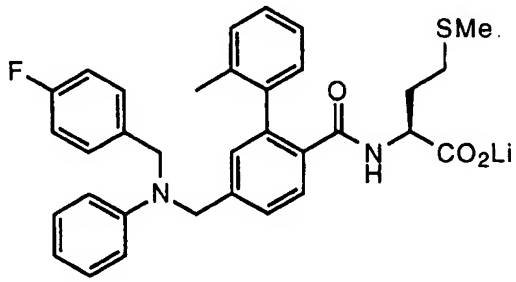
N-[4-N-(N-phenyl-N-(4-fluorobenzyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine lithium salt



Example 1238A

N-[4-N-(N-phenyl-N-(4-fluorobenzyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine, methyl ester

Prepared according to the procedure of 1236A from reaction between 1236C and 4-fluorobenzyl bromide. NMR($CDCl_3$) 7.85-7.95 (m, 1H); 7.15-7.4 (m, 9H); 6.95-7.15 (m, 3H); 6.7-6.8 (m, 3H); 5.8-5.9 (m, 1H); 4.70 (s, 2H); 4.58-4.65 (m, 3H); 3.62 (s, 3H); 2.0-2.15 (m, 8H); 1.7-2.0 (m, 1H); 1.5-1.7 (m, 1H). (DSI/NH_3)/MS: 571$(M+H)^+$.

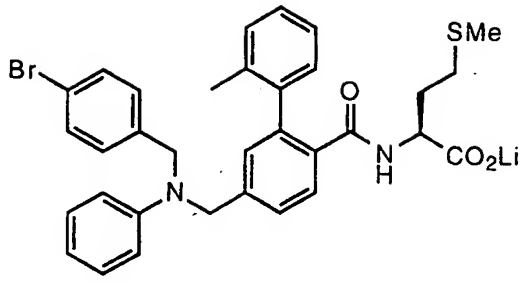


Example 1238B

N-[4-N-(N-phenyl-N-(4-fluorobenzyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine lithium salt

Prepared according to the procedure of example 1178J from 1238A. NMR ^1H(MeOH-d4): 7.6-7.7 (2H, m); 6.86-7.4 (10H, m); 6.6-6.85 (4H, m); 4.65-4.85 (4H, m); 4.18-4.3 (1H, m); 1.6-2.2 (10H, m). ESI(-)/MS: 555(M-Li).

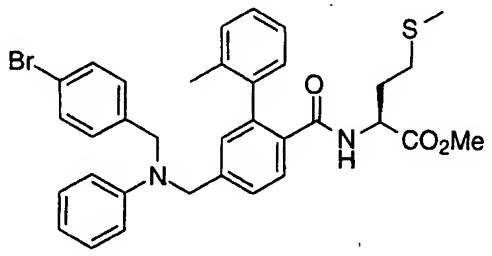
15450



Example 1239

N-[4-N-(N-phenyl-N-(4-bromobenzyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine lithium salt

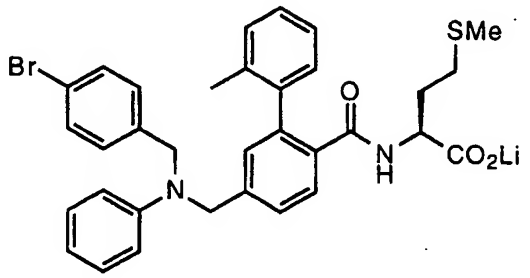
15455



Example 1239A

N-[4-N-(N-phenyl-N-(4-bromobenzyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine, methyl ester

15460 Prepared according to the procedure of example 1236A from reaction between 1236C and 4-bormobenzyl bromide. NMR($CDCl_3$) 7.85-7.95 (m, 1H); 7.05-7.48 (m, 12H); 6.65-6.78 (m, 3H); 5.8-5.9 (m, 1H); 4.75 (s, 2H); 4.55-4.65 (m, 3H); 3.65 (s, 3H); 2.0-2.15 (m, 8H); 1.7-2.0 (m, 1H); 1.5-1.7 (m, 1H). (DSI/NH_3)/MS: 631$(M+H)^+$.

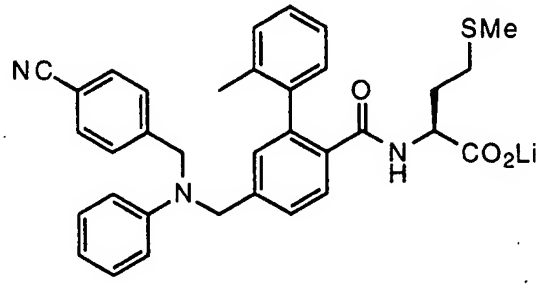


15465

Example 1239B

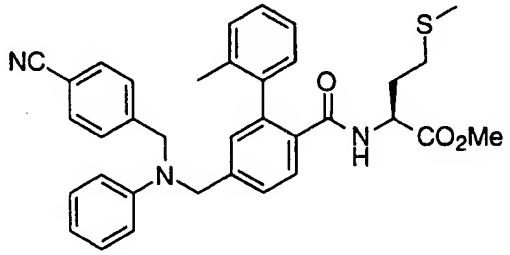
N-[4-N-(N-phenyl-N-(4-bromobenzyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine lithium salt

Prepared according to the procedure of example 1178J from 1239A. NMR ^{1}H(MeOH-d4): 7.58-7.67 (1H, d); 7.38-7.46 (2H, d); 7.3-7.39 (H, d); 7.0-7.3 (11H, m); 6.6-6.8 (3H, m); 4.75 (2H, s); 4.65 (2H, s); 4.18-4.3 (1H, m); 1.5-2.2 (10H, m). ESI(-)/MS: 615(M-Li), 573.



Example 1240

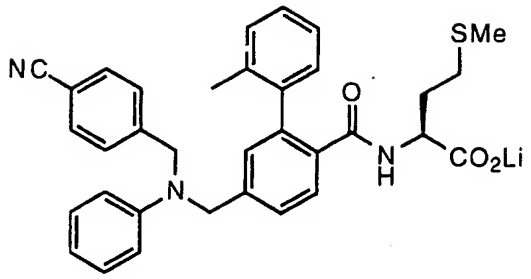
N-[4-N-(N-phenyl-N-(4-cyanobenzyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine lithium salt



Example 1240A

N-[4-N-(N-phenyl-N-(4-cyanobenzyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine, methyl ester

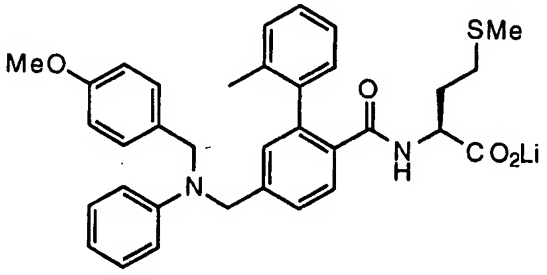
Prepared according to the procedure of example 1236A from reaction between 1236C and 4-cyanobenzyl bromide. NMR($CDCl_3$) 7.85-7.95 (m, 1H); 7.58-7.65 (m, 2H); 7.1-7.4 (m, 10H); 6.65-6.80 (m, 3H); 5.8-5.9 (m, 1H); 4.65 (m, 4H); 4.58-4.64 (m, 1H); 3.65 (s, 3H); 2.0-2.15 (m, 8H); 1.7-2.0 (m, 1H); 1.5-1.7 (m, 1H). (DSI/NH_3)/MS: 578$(M+H)^+$.



Example 1240B

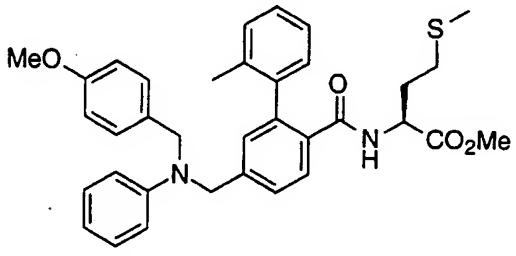
N-[4-N-(N-phenyl-N-(4-cyanobenzyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine lithium salt

Prepared according to the procedure of example 1178J from 1240A. NMR ^{1}H(MeOH-d4): 7.6-7.7 (3H, m); 7.4-7.5 (2H, m); 7.35-7.4 (1H, m); 7.02-7.3 (10H, m); 6.6-6.7 (3H, m) 4.9 (2H, s); 4.75 (2H, s); 4.18-4.3 (1H, m); 1.5-2.2 (10H, m). ESI(-)/MS: 562(M-Li).



Example 1241

N-[4-N-(N-phenyl-N-(4-methoxybenzyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine lithium salt

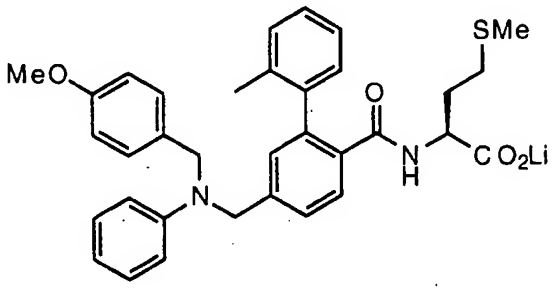


Example 1241A

N-[4-N-(N-phenyl-N-(4-methoxybenzyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine, methyl ester

Prepared according to the procedure of example 1236A from reaction between 1236C and 4-methoxybenzyl bromide. NMR($CDCl_3$) 7.85-7.95 (m, 1H); 7.15-7.4 (m,

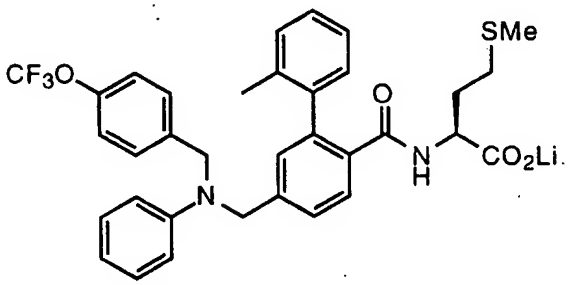
12H); 6.8-6.9 (m, 1H); 6.7-6.8 (m, 2H); 5.8-5.9 (m, 1H); 4.65 (m, 3H); 4.60 (s, 2H); 3.81 (s, m); 3.65 (s, 3H); 2.0-2.15 (m, 8H); 1.7-2.0 (m, 1H); 1.5-1.7 (m, 1H). (DSI/NH_3)/MS: 583$(M+H)^+$.



Example 1241B

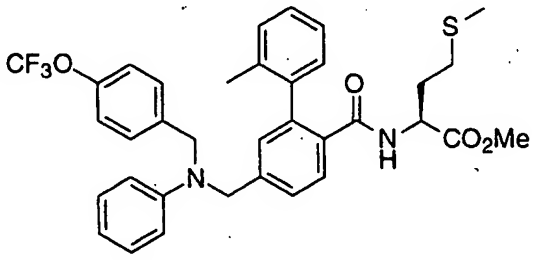
N-[4-N-(N-phenyl-N-(4-methoxybenzyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine lithium salt

Prepared according to the procedure of example 1178J from 1241A. NMR ^1H(MeOH-d_4): 7.6-7.7 (1H, m); 7.0-7.3 (10H, m); 6.6-6.85 (6H, m); 4.68 (2H, s); 4.58 (2H, s); 4.18-4.3 (1H, m); 3.88 (3H, s); 1.5-2.2 (10H, m). ESI(-)/MS: 567(M-Li); 445.



Example 1242

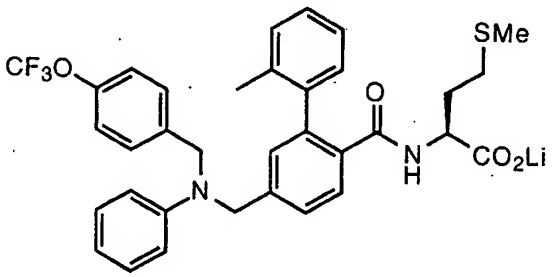
N-[4-N-(N-phenyl-N-(4-trifluoromethoxybenzyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine lithium salt



Example 1242A

N-[4-N-(N-phenyl-N-(4-trifluoromethoxybenzyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine, methyl ester

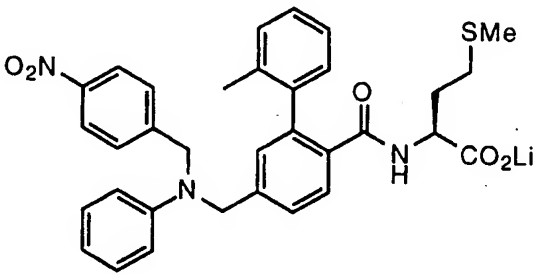
Prepared according to the procedure of example 1236A from reaction between 1236C and 4-trifluoromethoxybenzyl bromide. NMR($CDCl_3$) 7.85-7.95 (m, 1H); 7.15-7.4 (m, 12H); 6.8-6.9 (m, 1H); 6.7-6.8 (m, 2H); 5.8-5.9 (m, 1H); 4.65 (m, 3H); 4.60 (s, 2H); 3.65 (s, 3H); 2.0-2.15 (m, 8H); 1.7-2.0 (m, 1H); 1.5-1.7 (m, 1H). (DSI/NH_3)/MS: 636$(M+H)^+$.



Example 1242B

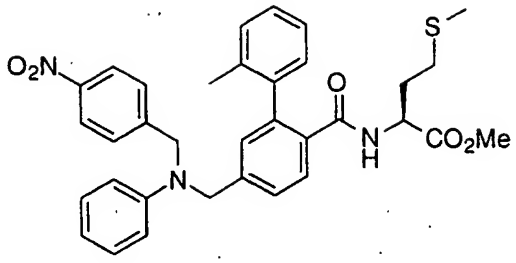
N-[4-N-(N-phenyl-N-(4-trifluoromethoxybenzyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine lithium salt

Prepared according to the procedure of example 1178J from 1242A. NMR ^1H(MeOH-d4): 7.6-7.7 (1H, m); 7.3-7.4 (3H, d), 7.05-7.25 (9H, m); 6.7-6.8 (2H, m); 6.6-6.7 (1H, m); 4.7-4.8 (4H, m); 4.1-4.22 (1H, m); 1.7-2.1 (10H, m). ESI(-)/MS: 621(M-Li).



Example 1243

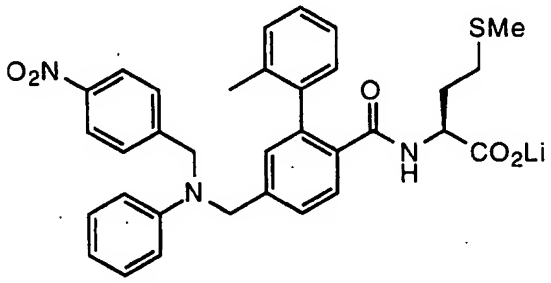
N-[4-N-(N-phenyl-N-(4-nitrobenzyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine lithium salt



Example 1243A

N-[4-N-(N-phenyl-N-(4-nitrobenzyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine, methyl ester

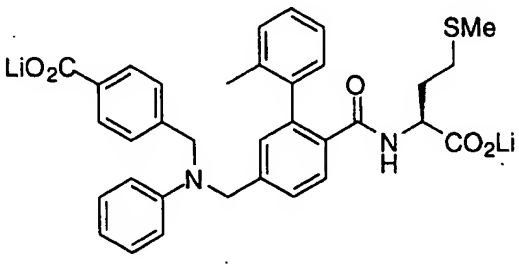
Prepared according to the procedure of example 1236A from reaction between 1236C and 4-nitrobenzyl bromide. NMR($CDCl_3$) 8.15-8.20 (m, 2H); 7.85-7.95 (m, 1H); 7.1-7.45 (m, 10H); 6.75-6.81 (m, 1H); 6.65-6.71 (m, 2H); 5.78-5.88 (m, 1H); 4.7-4.8 (ss, 4H); 4.6-4.75 (m, 1H); 3.65 (s, 3H); 2.0-2.15 (m, 8H); 1.7-2.0 (m, 1H); 1.5-1.7 (m, 1H). (DSI/NH_3)/MS: 598$(M+H)^+$; 615 $(M+NH_4)^+$.



Example 1243B

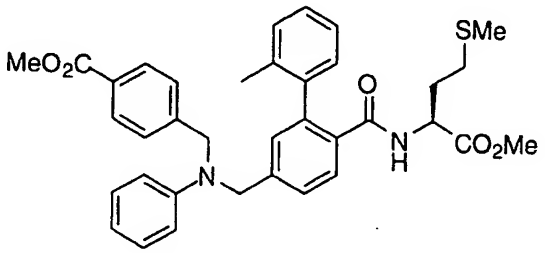
N-[4-N-(N-phenyl-N-(4-nitrobenzyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine lithium salt

Prepared according to the procedure of example 1178J from 1243A. NMR ^1H(MeOH-d4): 8.15-8.2 (2H, m); 7.6-7.7 (1H, m), 7.48-7.56 (2H, m); 7.35-7.41 (1H, m); 7.15-7.3 (8H, m); 6.65-6.78 (3H, m), 4.78-4.85(4H, m); 4.1-4.22 (1H, m); 1.7-2.1 (10H, m). ESI(-)/MS: 582(M-Li).



Example 1244

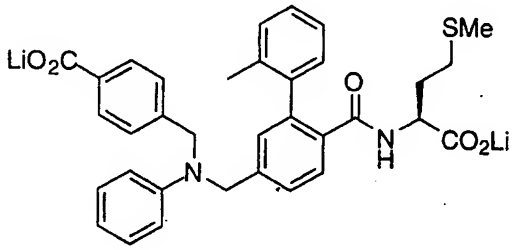
N-[4-N-(N-phenyl-N-(4-carboxylic acid benzyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine, dilithium salt



Example 1244A

N-[4-N-(N-phenyl-N-(4-carboxylic acid benzyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine, dimethyl ester

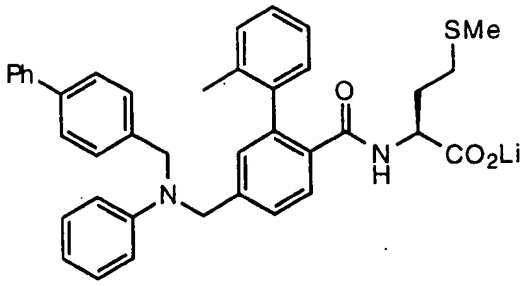
Prepared according to the procedure of example 1236A from reaction between 1236C and methyl 4-(bromomethyl) benzyolate. NMR($CDCl_3$) 7.85-7.95 (m, 1H); 7.18-7.40 (m, 12H; 6.7-6.85 (m, 3H); 5.8-5.9 (m, 1H); 4.7 (s, 4H); 4.58-4.68 (m, 1H); 3.90 (s, 3H); 3.68 (s, 3H); 2.0-2.15 (m, 8H); 1.7-2.0 (m, 1H); 1.5-1.7 (m, 1H). (DSI/NH_3)/MS: 628$(M+NH_4)^+$.



Example 1244B

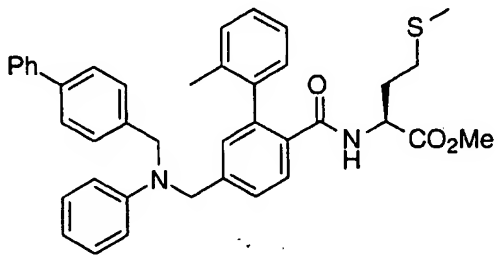
N-[4-N-(N-phenyl-N-(4-carboxylic acid benzyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine, dilithium salt

Prepared according to the procedure of example 1178J from 1244A. NMR ^1H(MeOH-d4): 7.9-8.0 (2H, m); 7.6-7.7 (1H, m), 7.3-7.4 (2H, m); 7.1-7.28 (9H, m); 6.7-6.75 (2H, m); 6.6-6.7 (1H, m); 4.78 (2H, s); 4.70 (2H, s); 4.1-4.22 (1H, m); 1.7-2.1 (10H, m). ESI(-)/MS: 595(M-Li).



Example 1245

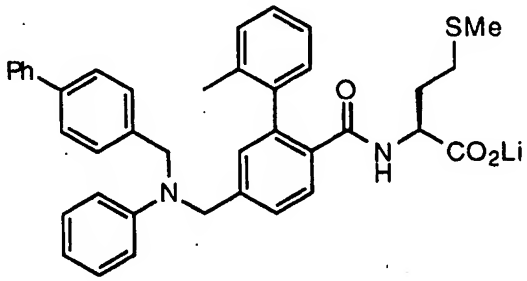
N-[4-N-(N-phenyl-N-(4-phenylbenzyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine lithium salt



Example 1245 A

N-[4-N-(N-phenyl-N-(4-phenylbenzyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine, methyl ester

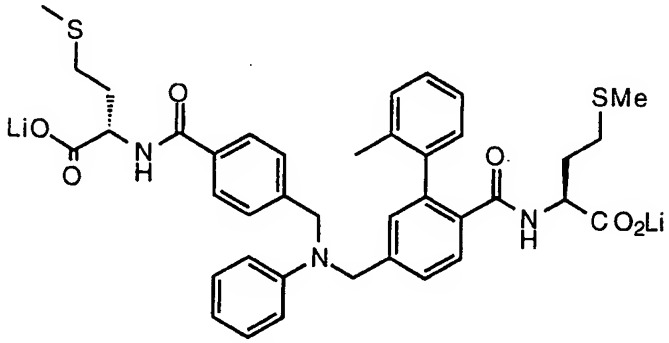
Prepared according to the procedure of example 1236A from reaction between 1236C and 4-phenylbenzyl bromide. NMR($CDCl_3$) 7.85-7.95 (m, 1H); 7.1-7.45 (m, 17H); 6.75-6.81 (m, 1H); 6.65-6.7 (m, 3H); 5.8-5.9 (m, 1H); 4.7-4.8 (ss, 4H); 4.6-4.75 (m, 1H); 3.65 (s, 3H); 2.0-2.15 (m, 8H); 1.7-2.0 (m, 1H); 1.5-1.7 (m, 1H). (DSI/NH_3)/MS: 629$(M+H)^+$.



Example 1245B

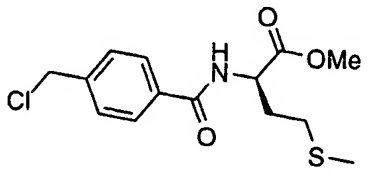
N-[4-N-(N-phenyl-N-(4-phenylbenzyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine lithium salt

Prepared according to the procedure of example 1178J from 1245A. NMR ^{1}H(MeOH-d4): 7.1-7.7 (19H, m); 6.7-6.8 (2H, m); 6.6-6.7 (1H, m); 4.7-4.8 (4H, m); 4.1-4.22 (1H, m); 1.7-2.1 (10H, m). ESI(-)/MS: 613(M-Li).



Example 1246

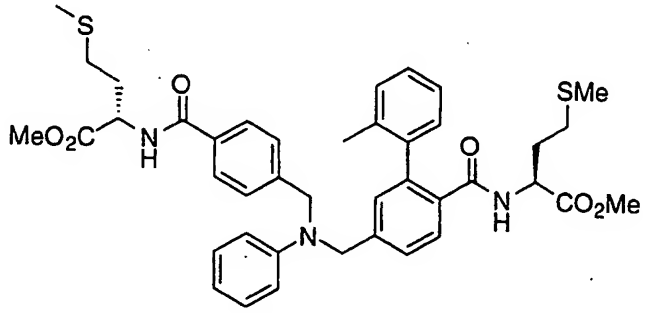
N-[4-N-(N-phenyl-N-(4-N-carboxymethionine)benzyl)aminomethyl-2-(2-methylphenyl)benzoyl]methionine dilithium salt.



Example 1246A

4-(chloromethyl)-benzoylmethionine, methyl ester

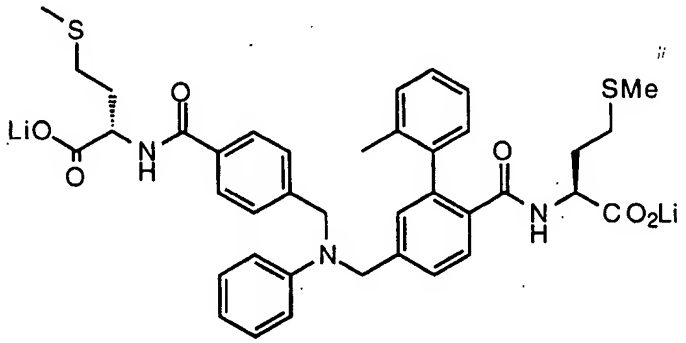
A mixture of 4-(chloromethyl)-benzoyl chloride (0.189 g, 1 mmol), methionine methyl ester hydrochloride (0.199 g, 1 mmol), and 0.5 ml of pyridine in 5 ml of chloroform was stirred for 12 hours. The organic solution was washed with 10 % HCl, brine, and dried over $MgSO_4$. Flash chromatography of the residue afforded 0.20 g of desired product (64%). NMR($CDCl_3$) 7.80-7.85 (m, 2H); 7.28-7.32 (m, 2H; 6.9-7.0 (m, 1H); 4.9-5.0 (m, 1H); 4.60 (s, 2H); 3.80 (s, 3H); 3.68 (s, 3H); 2.35-2.45 (m, 2H); 2.12-2.35 (m, 1H); 2.1-2.2 (m, 1H). (DSI/NH_3)/MS: 316$(M+H)^+$; 333$(M+NH_4)^+$.



Example 1246B

N-[4-N-(N-phenyl-N-(4-N-carboxymethionine)benzyl)aminomethyl-2-(2-methylphenyl)benzoyl]methionine, dimethyl ester

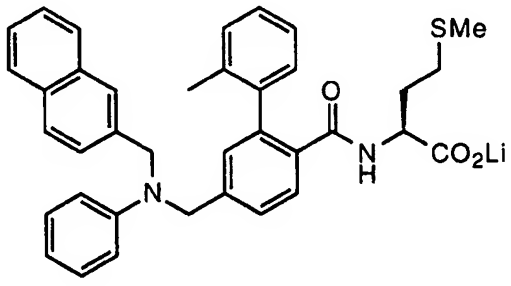
Prepared according to the procedure of example 1236A from the reaction between 1236C and 1246A. NMR($CDCl_3$) 7.85-7.95 (m, 1H); 7.75-7.80 (m, 2H); 7.18-7.35 (m, 9H); 7.10 (s, 1H); 6.9-6.95 (m, 1H); 6.68-6.78 (m, 3H); 5.8-5.9 (m, 1H); 4.81 (s, 2H); 4.5-4.65 (m, 1H); 3.80 (s, 3H); 3.68 (s, 3H); 2.35-2.45 (m, 2H); 2.12-2.35 (m, 1H);); 2.0-2.15 (m, 9H); 1.7-2.0 (m, 1H); 1.5-1.7 (m, 1H). (DSI/NH_3)/MS: 742$(M+H)^+$.



Example 1246C

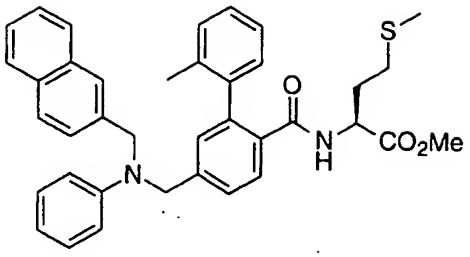
N-[4-N-(N-phenyl-N-(4-N-carboxymethionine)benzyl)aminomethyl-2-(2-methylphenyl)benzoyl]methionine dilithium salt.

Prepared according to the procedure of example 1178J from 1246B. NMR ^1H (d_4-MeOH): 7.8-7.9 (2H, m); 7.6-7.7 (1H, m); 7.3-7.4 (4H, m); 7.2 (4H, m); 7.1 (4H, m); 6.7-6.75 (2H, m); 6.6-6.7 (1H, m); 4.8 (4H, m); 4.5-4.6 (1H, m); 4.2-4.3 (1H, m); (2.5-2.65 (2H, m); 1.6-2.3 (15H, m). ESI(-)/MS: 711 (M-Li); 733 (M+Na-2H).



Example 1247

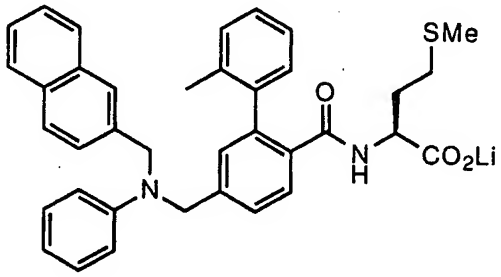
N-[4-N-(N-phenyl-N-(2-naphthyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine lithium salt



Example 1247A

N-[4-N-(N-phenyl-N-(2-naphthyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine, methyl ester

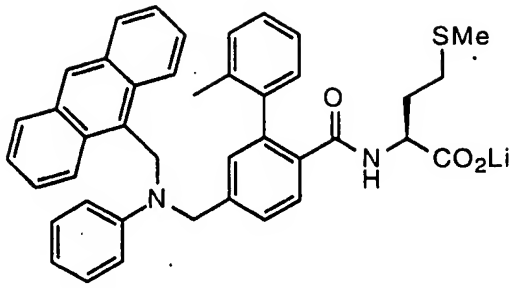
Prepared according to the procedure of example 1236A from reaction between 1236C and 2-bromomethyl-naphthalene. NMR($CDCl_3$) 7.68-7.95 (m, 5H); 7.18-7.45 (m, 11H); 7.1 (s, 1H); 6.7-6.85 (m, 3H); 5.8-5.9 (m, 1H); 4.80 (s, 2H); 4.76 (s, 2H); 4.56-4.7 (m, 1H); 3.68 (s, 3H); 2.0-2.15 (m, 8H); 1.7-2.0 (m, 1H); 1.5-1.7 (m, 1H). (DSI/NH_3)/MS: 603$(M+H)^+$.



Example 1247B

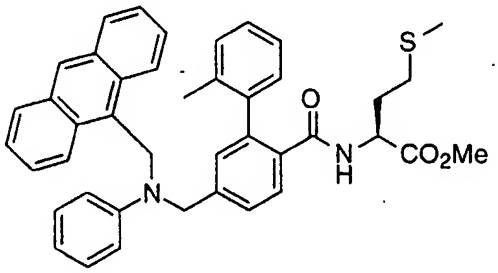
N-[4-N-(N-phenyl-N-(2-naphthyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine lithium salt

Prepared according to the procedure of example 1178J from 1247A. NMR ^1H(MeOH-d4): 7.78-7.84 (2H, m); 7.6-7.8 (3H, m), 7.3-7.5 (4H, d); 7.0-7.25 (8H, m); 6.8-7.0 (2H, m); 6.75-6.82 (2H, m); 6.6-6.6 (1H, m); 4.8 (2H, s); 4.85 (2H, s); 4.1-4.22 (1H, m); 1.7-2.1 (10H, m). ESI(-)/MS: 587(M-Li).



Example 1248

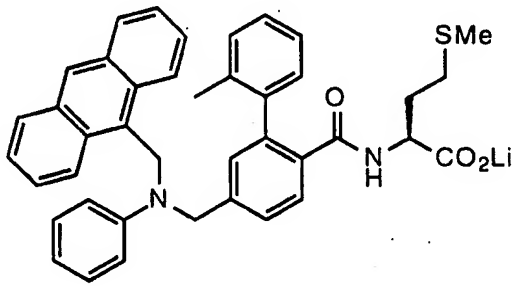
N-[4-N-(N-phenyl-N-(9-methyl-anthracene-yl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine lithium salt



Example 1248A

N-[4-N-(N-phenyl-N-(9-methyl-anthracene-yl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine, methyl ester

Prepared according to the procedure of example 1236A from reaction between 1236C and 9-bromomethyl-anthracene. NMR($CDCl_3$) 8.4 (s, 1H); 8.1-8.2 (m, 2H); 7.9-8.0 (m, 2H); 7.0-7.65 (m, 12H); 7.1 (s, 1H); 6.8-6.95 (m, 3H); 5.8-5.9 (m, 1H); 5.45 (s, 2H); 4.68 (m, 1H); 4.25 (s, 2H); 3.60 (s, 3H); 2.0-2.15 (m, 8H); 1.7-2.0 (m, 1H); 1.5-1.7 (m, 1H). (DSI/NH_3)/MS: 653$(M+H)^+$.

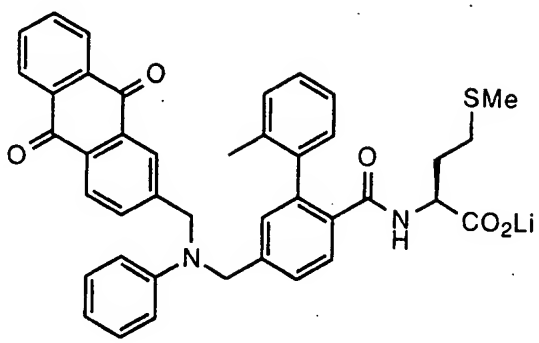


Example 1248B

N-[4-N-(N-phenyl-N-(9-methyl-anthracene-yl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine lithium salt

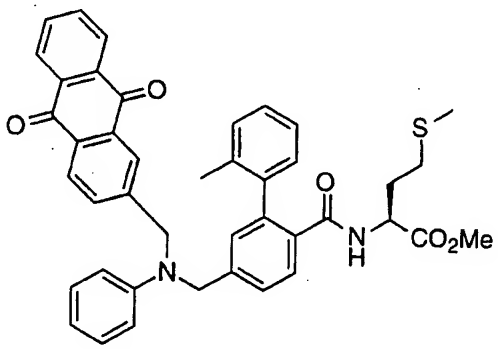
Prepared according to the procedure of example 1178J from 1248A. NMR ^1H(MeOH-d4): 8.45 (1H, s); 8.17-8.22 (2H, m), 7.9-8.05 (2H, m); 7.1-7.5 (13H, m),

6.8-6.95 (3H, m); 6.5-6.67 (1H, m); 5.45 (2H, s); 4.5 (2H, s); 4.1-4.22 (1H, m); 1.7-2.1 (10H, m). ESI(-)/MS: 637(M-Li).



Example 1249

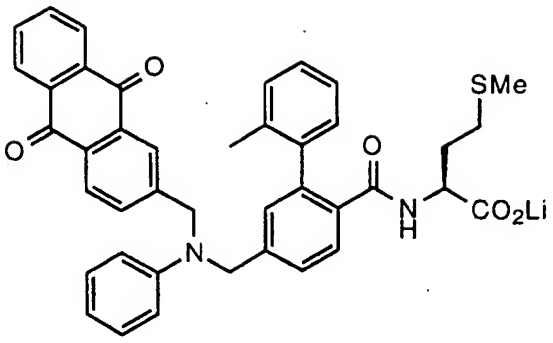
N-[4-*N*-(*N*-phenyl-*N*-(2-methyl-anthraquinone-yl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine lithium salt



Example 1249A

N-[4-*N*-(*N*-phenyl-*N*-(2-methyl-anthraquinone-yl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine, methyl ester

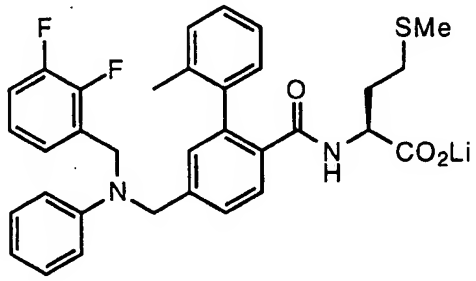
Prepared according to the procedure of example 1236A from reaction between 1236C and 2-bromomethyl-anthraquinone. NMR($CDCl_3$) 8.4 (s, 1H); 8.0-8.35 (m, 3H); 7.9-8.0 (m, 2H); 7.0-7.65 (m, 11H); 6.8-6.95 (m, 3H); 5.8-5.9 (m, 1H); 4.8 (s, 2H); 4.78 (s, 2H); 4.56-4.7 (m, 1H); 3.63 (s, 3H); 2.0-2.15 (m, 8H); 1.7-2.0 (m, 1H); 1.5-1.7 (m, 1H). (DSI/NH_3)/MS: 683$(M+H)^+$.



Example 1249B

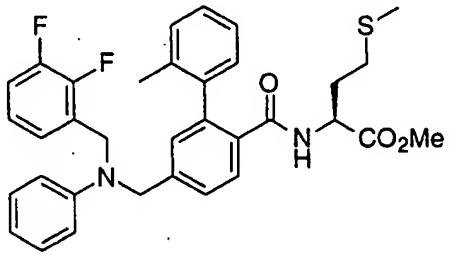
N-[4-*N*-(*N*-phenyl-*N*-(2-methyl-anthraquinone-yl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine lithium salt

Prepared according to the procedure of example 1178J from 1249A. NMR ^{1}H(MeOH-d4): 8.1-8.3 (4H, m); 7.8-7.9 (2H, m), 7.7-7.8 (1H, m); 7.6-7.7 (1H, m); 7.25-7.35 (1H, m); 7.0-7.3 (8H, m); 6.75-6.8 (2H, m); 6.6-6.7 (1H, m); 4.9 (2H, s); 4.8 (2H, s); 4.1-4.22 (1H, m); 1.7-2.1 (10H, m). ESI(-)/MS: 667(M-Li).



Example 1250

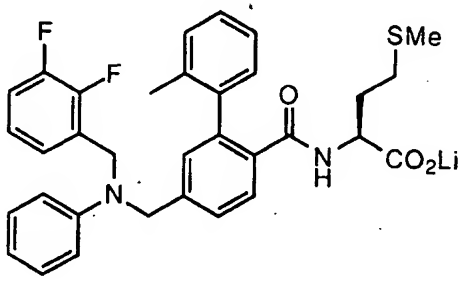
N-[4-*N*-(*N*-phenyl-*N*-(2,3-difluorobenzyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine lithium salt



Example 1250A

N-[4-*N*-(*N*-phenyl-*N*-(2,3-difluorobenzyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine, methyl ester

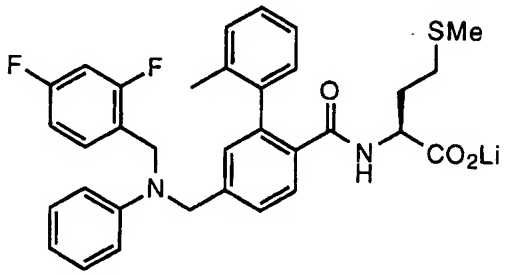
Prepared according to the procedure of example 1236A from reaction between 1236C and 2,3-difluorobenzyl bromide. NMR($CDCl_3$) 7.85-7.95 (m, 1H); 6.95-7.40 (m, 11H); 6.68-6.8 (m, 3H); 5.8-5.9 (m, 1H); 4.75 (s, 2H); 4.70 (s, 2H); 4.60-4.70 (m, 1H); 3.70 (s, 3H); 2.0-2.15 (m, 8H); 1.7-2.0 (m, 1H); 1.5-1.7 (m, 1H). (DSI/NH_3)/MS: 589$(M+H)^+$.



Example 1250B

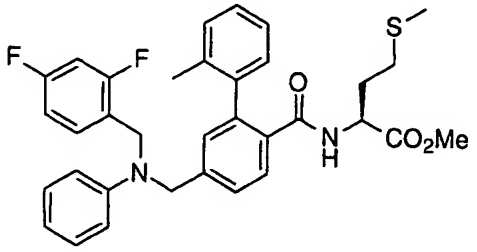
N-[4-*N*-(*N*-phenyl-*N*-(2,3-difluorobenzyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine lithium salt

Prepared according to the procedure of example 1178J from 1250A. NMR ^1H(MeOH-d4): 7.7-7.8 (1H, m); 7.3-7.4 (1H, m), 7.0-7.28 (11H, m); 6.65-6.75 (3H, m); 4.8-4.85 (4H, m); 4.1-4.22 (1H, m); 1.7-2.1 (10H, m). ESI(-)/MS: 573(M-Li).



Example 1251

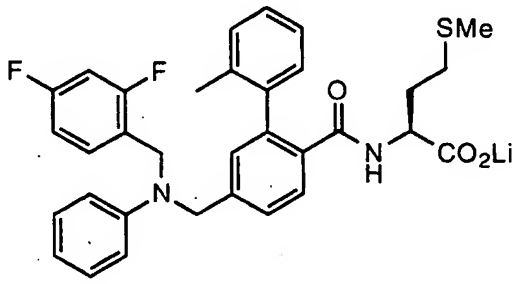
N-[4-*N*-(*N*-phenyl-*N*-(2,4-difluorobenzyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine lithium salt



Example 1251A

N-[4-*N*-(*N*-phenyl-*N*-(2,4-difluorobenzyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine, methyl ester

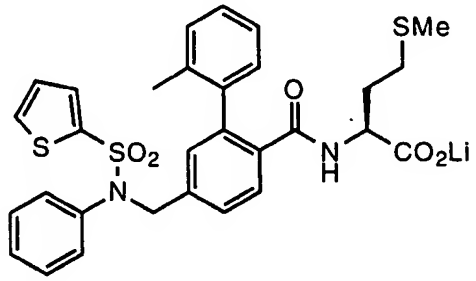
Prepared according to the procedure of example 1236A from reaction between 1236C and 2,4-difluorobenzyl bromide. NMR($CDCl_3$) 7.85-7.95 (m, 1H); 7.18-7.40 (m, 9H); 7.1 (s, 1H); 6.7-6.85 (m, 4H); 5.8-5.9 (m, 1H); 4.7 (s, 2H); 4.68 (m, 3H); 3.68 (s, 3H); 2.0-2.15 (m, 8H); 1.7-2.0 (m, 1H); 1.5-1.7 (m, 1H). (DSI/NH_3)/MS: 589$(M+H)^+$.



Example 1251B

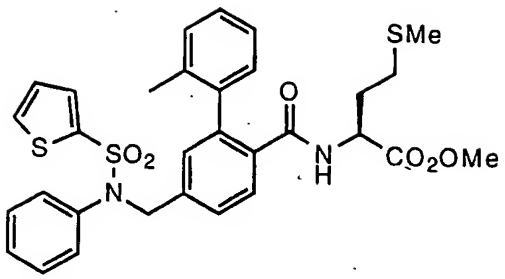
N-[4-*N*-(*N*-phenyl-*N*-(2,4-difluorobenzyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine lithium salt

Prepared according to the procedure of example 1178J from 1251A. NMR ^1H(MeOH-d4): 7.6-7.68 (1H, m); 7.3-7.4 (1H, m), 7.3-7.4 (1H, d); 7.0-7.3 (9H, m); 6.8-7.0 (2H, m); 6.6-6.8 (3H, m); 4.70 (2H, s); 4.75 (2H, s); 4.1-4.22 (1H, m); 1.7-2.1 (10H, m). ESI(-)/MS: 573(M-Li).



Example 1255

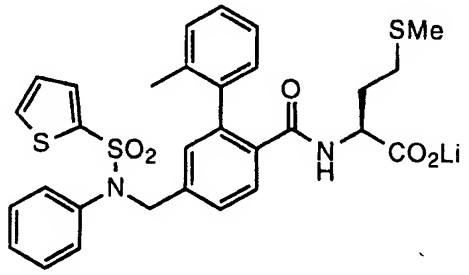
N-[4-*N*-(*N*-phenyl-*N*-(2-thiophenesulfonyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine lithium salt



Example 1255A

15790 *N*-[4-*N*-(*N*-phenyl-*N*-(2-thiophenesulfonyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine, methyl ester

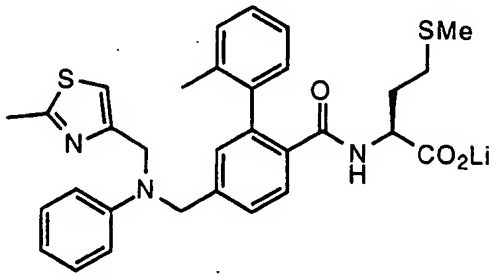
Prepared according to the procedure of example 1229A from reaction between 1236C and 2-thiophenesulfonyl chloride. NMR($CDCl_3$) 7.75-7.82 (m, 1H); 7.60-7.62 (m, 1H); 7.39-7.42 (m, 1H); 7.12-7.38 (m, 9H); 7.05-7.11 (m, 2H); 6.95-7.05 (m, 2H); 5.8-
15795 5.9 (m, 1H); 4.78 (s, 2H); 4.5-4.65 (m, 1H); 3.62 (s, 3H); 2.0-2.15 (m, 8H); 1.7-2.0 (m, 1H); 1.5-1.7 (m, 1H). (DSI/NH_3)/MS: 609$(M+H)^+$; 626$(M+NH_4)^+$.



Example 1255B

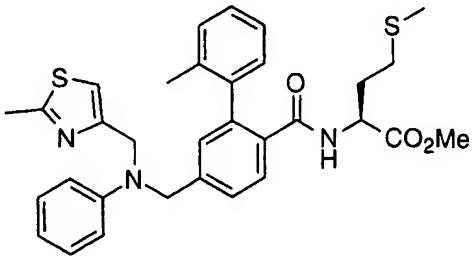
15800 *N*-[4-*N*-(*N*-phenyl-*N*-(2-thiophenesulfonyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine lithium salt

Prepared according to the procedure of example 1178J from 1255A. NMR ^1H(MeOH-d4): 7.8-7.9 (1H, m); 7.5-7.6 (1H, m), 7.42-7.45 (1H, m); 7.1-7.3 (9H, m); 6.95-7.1 (3H, m); 4.9 (2H, s); 4.1-4.22 (1H, m); 1.7-2.1 (10H, m). ESI(-)/MS: 593(M-
15805 Li).



Example 1256

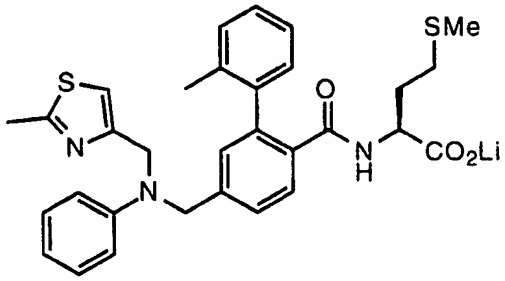
N-[4-*N*-(*N*-phenyl-*N*-(2-methyl-4-methylenethiazolyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine lithium salt



Example 1256A

N-[4-*N*-(*N*-phenyl-*N*-(2-methyl-4-methylenethiazolyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine, methyl ester

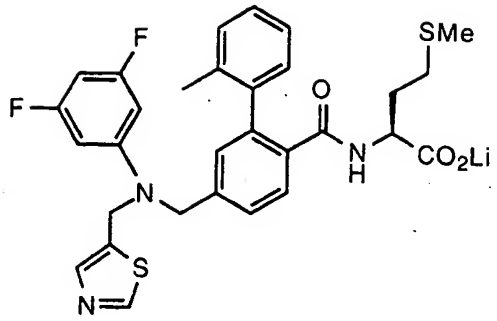
Prepared according to the procedure of example 1236A from reaction between 1236C and 4-methyl-2-(bromomethyl)-thiazole. NMR($CDCl_3$) 7.82-7.95 (m, 1H); 7.10-7.40 (m, 9H); 6.8 (s, 1H); 6.7-6.8 (m, 2H); 5.8-5.9 (m, 1H); 4.78 (s, 2H); 4.75 (s, 2H); 4.56-4.7 (m, 1H); 3.68 (s, 3H); 2.67 (s, 3H); 2.0-2.15 (m, 8H); 1.7-2.0 (m, 1H); 1.5-1.7 (m, 1H). (DSI/NH_3)/MS: 574$(M+H)^+$.



Example 1256B

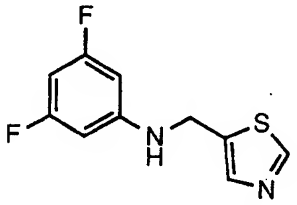
N-[4-*N*-(*N*-phenyl-*N*-(2-methyl-4-methylenethiazolyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine lithium salt

Prepared according to the procedure of example 1178J from 1256A. NMR ^1H(MeOH-d4): 7.6-7.68 (1H, m); 7.32-7.4 (1H, m), 7.0-7.28 (9H, m); 6.7-6.8 (2H, m); 6.6-6.7 (1H, m); 4.78 (2H, s); 4.70 (2H, s); 4.1-4.22 (1H, m); 2.62 (3H, s); 1.7-2.1 (10H, m). ESI(-)/MS: 558(M-Li).



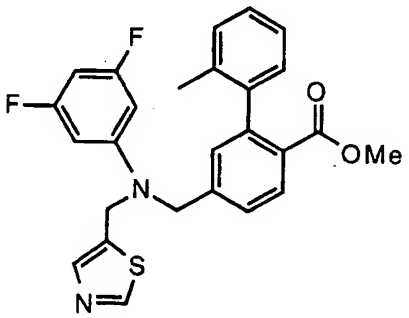
Example 1257

15835 *N*-[4-*N*-(*N*-3,5-difluorophenyl-*N*-(5-thiazolylmethyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine lithium salt.



Example 1257A

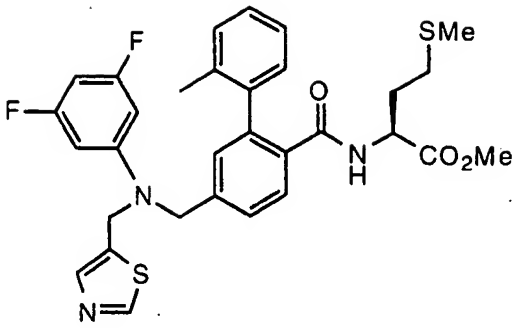
15840 Prepared according to the procedure of example 1258A from reaction between 3,5-difluoroaniline and 5-thizaolecarboxaldehyde. NMR($CDCl_3$) 8.85 (s, 1H); 7.82 (s, 1H); 6.10-6.30 (m, 3H); 4.56 (s, 2H); 4.05-4.50 (m, 1H). DSI/NH_3)/MS: 227$(M+H)^+$; 244$(M+NH_4)^+$.



15845

Example 1257B

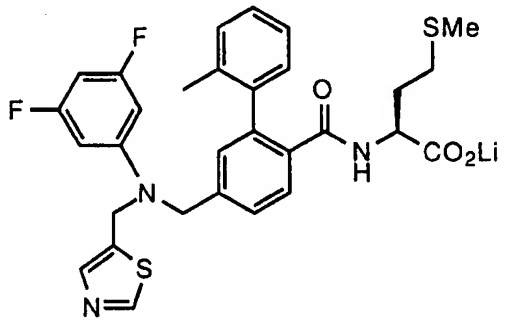
Prepared according to the procedure of example 1287B from reaction between 1257A and 4-bromomethyl-2-(2-methylphenyl)benzoic acid methyl ester. NMR($CDCl_3$) 8.75-8.80 (s, 1H); 7.82-8.00 (m, 1H); 7.75 (s, 1H); 7.12-7.38 (m, 4H); 7.00-7.10 (m,
15850 2H); 6.20-6.27 (m, 3H); 4.80 (s, 2H); 4.60 (s, 2H); 3.60 (s, 3H); 2.03 (s, 3H). DSI/NH_3)/MS: 465$(M+H)^+$; 482$(M+NH_4)^+$.



Example 1257C

N-[4-*N*-(*N*-3,5-difluorophenyl-*N*-(5-thiazolylmethyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine, methyl ester.

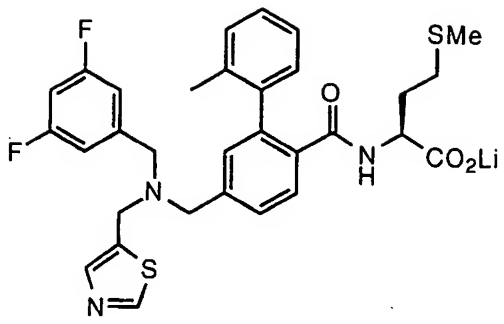
Prepared according to the procedure of example 1258C from 1257B. NMR($CDCl_3$) 8.75-8.80 (s, 1H); 7.80-7.90 (m, 1H); 7.65-7.80 (m, 1H); 7.12-7.38 (m, 5H); 6.93 (s, 1H); 6.10-6.20 (m, 3H); 4.68 (s, 2H); 4.48-4.60 (m, 3H); 3.57 (s, 3H); 1.90-2.10 (m, 8H); 1.60-1.90 (m, 1H); 1.45-1.60 (m, 1H). DSI/NH_3)/MS: 596$(M+H)^+$.



Example 1257D

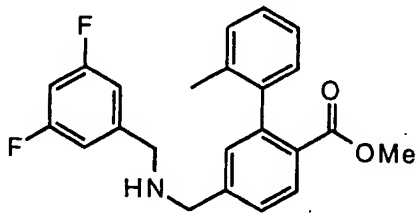
N-[4-*N*-(*N*-3,5-difluorophenyl-*N*-(5-thiazolylmethyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine lithium salt.

Prepared according to the procedure of example 1178J from 1257C. ^1H NMR (MeOH-d_4): 8.9 (1H, s); 7.8 (1H, s); 7.6-7.7 (1H, m); 7.3-7.4 (1H, m); 7.1-7.3 (3H, m); 7.0-7.1 (1H, s); 6.3-6.45 (2H, m); 6.2-6.3 (1H, s); 4.95 (2H, s); 4.7 (2H, s); 4.1-4.22 (1H, m); 1.6-2.2 (10H, m). ESI(-)/MS: 580(M-Li). Anal. Calcd for $C_{30}H_{28}F_2N_3O_3S_2Li \cdot 1.73H_2O$: C, 58.23; H, 5.12; N, 6.79. Found: C, 58.24; H, 4.90; N, 6.54.



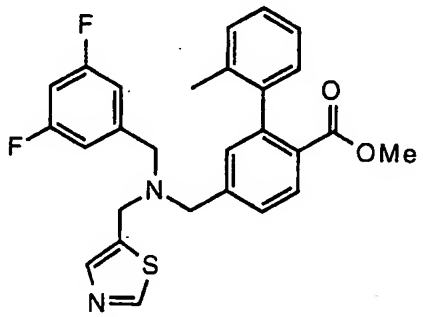
Example 1258

N-[4-*N*-(*N*-(5-thiazolylmethyl)-*N*-(3,5-difluorobenzyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine lithium salt.



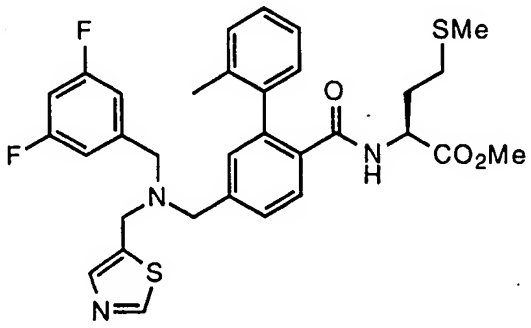
Example 1258A

A mixture of 3,5-difluorobenzyl amine (2.0 g, 14.2 mmol), 4-formyl-2-(2-methylphenyl)benzoic acid methyl ester (3.6 g, 14.2 mmol), and sodium triacetoxyborohydride (6.0 g, 28.8 mmol) in 50 ml of 1,2-dichloroethane was stirred for 24 hours. The reaction mixture was washed with 4N NaOH and with brine, then dried over anhydrous $MgSO_4$. Flash chromatography of the reside from evaporation of the organic solution eluting with 1:1 EtOAc/Hexane afforded 4.01 g of the title compound. (74%). NMR($CDCl_3$) 7.95-8.00 (m, 1H); 7.38-7.45 (m, 1H); 7.18-7.30 (m, 4H); 7.05-7.15 (m, 1H); 6.85-6.92 (m, 2H); 6.63-6.72 (m, 1H); 3.88 (s, 2H); 3.80 (s, 2H); 3.62 (s, 3H); 2.05 (s, 3H). (DSI/NH_3)/MS: 382$(M+H)^+$; 399$(M+NH_4)^+$.



Example 1258B

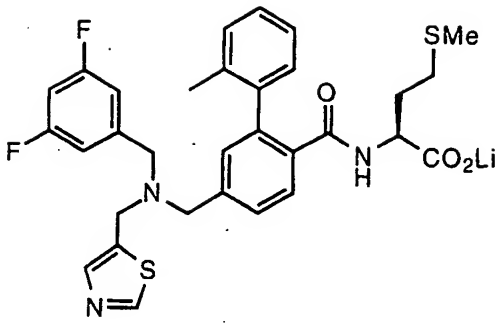
Prepared according to the procedure of example 1258A from reaction between 1258A and 5-thiazolealdehyde. NMR($CDCl_3$) 8.80 (s, 1H); 7.95-8.00 (m, 1H); 7.72 (s, 1H); 7.50-7.55 (m, 1H); 7.10-7.32 (m, 4H); 7.0-7.1 (m, 1H); 6.9-7.0 (m, 2H); 6.68-6.72 (m, 1H); 4.62-4.70 (m, 2H); 3.60 (s, 5H); 2.07 (s, 3H). (DSI/NH_3)/MS: 479$(M+H)^+$; 496$(M+NH_4)^+$.



Example 1258C

A mixture of 1258B (0.304 g, 0.63 mmol) and lithium hydroxide (0.076 g, 3.15 mmol) in 30 ml of 1:1 water/methanol was refluxed for 12 hours. After cooling to room temperature, the reaction mixture was neutralized to PH= 5-6 carefully by 1.0 M $NaHSO_4$. The precipitate from neutralization was extracted into 40 ml of EtOAc. The organic solution was then washed by brine, and dried over anhydrous $MgSO_4$. Evaporation of the solvent afforded pure corresponding acid which was used directly for methionine coupling reaction.

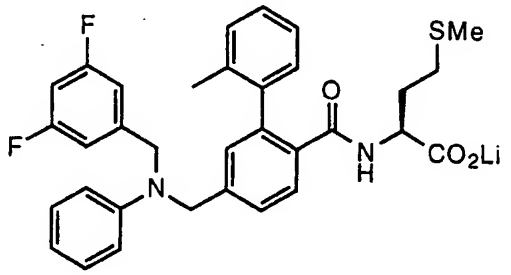
A mixture of the acid(0.30g, 0.63 mmol) from previous step, L-methionine methyl ester hydrochloride (0.252g, 1.26 mmol), 1-hydroxybenzotriazole hydrate (0.43 g, 3.15 mmol), 1-ethyl-3-(3-dimethyl-aminopropyl)carbodiimide (0.61 g, 3.15 mmol), and triethylamine hydrochloride (0.43 g, 3.15 mmol) in 15 ml of anhydrous DMF was heated under N_2 at 75°C for 20 hours. After cooling to room temperature, the solution was diluted with 50 ml of EtOAc, then was put to 200 ml of water. The aqueous solution was extracted with another portion of 50 ml of EtOAC. Combined organic solution was washed with 30 ml of saturated $NaHCO_3$ twice, then with 50 ml of brine, finally dried over anhydrous $MgSO_4$. Flash chromatography of the residue from evaporation of the EtOAc solution eluting with 70:30 EtOAc/Hexane afforded 0.235 g of the title compound. (61%). NMR($CDCl_3$) 8.78 (s, 1H); 7.90-8.00 (m, 1H); 7.72 (s, 1H); 7.50-7.55 (m, 1H); 7.20-7.38 (m, 5H); 6.9-7.0 (m, 2H); 6.68-6.72 (m, 1H); 5.88-5.92 (m, 2H); 4.58-4.70 (m, 1H); 3.88 (s, 2H); 4.62-4.70 (m, 5H); 3.60 (s, 2H); 2.0-2.15 (m, 8H); 1.7-2.0 (m, 1H); 1.5-1.7 (m, 1H). (DSI/NH_3)/MS: 610$(M+H)^+$.



Example 1258D

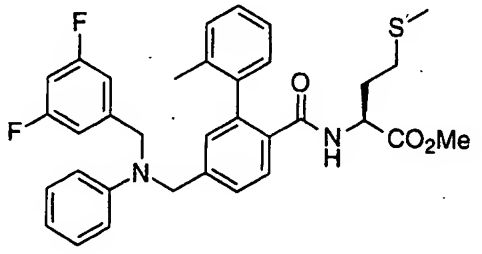
N-[4-*N*-(*N*-(5-thiazolylmethyl)-*N*-(3,5-difluorobenzyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine lithium salt.

Prepared according to the procedure of example of 1178J from example 1258C. NMR ^{1}H(MeOH-d4): 8.95 (1H, s); 7.78 (1H, s); 7.6-7.7 (1H, m); 7.4-7.5 (1H, m), 7.05-7.3 (5H, m); 6.95-7.05(2H, m); 6.85-6.95 (1H, m); 4.95 (2H, s); 4.1-4.22 (1H, m); 3.9 (2H, s); 4.7 (2H, m); 4.6 (2H, s); 2.25 (2H, s); 1.6-2.1 (8H, m). ESI(-)/MS: 594(M-Li).



Example 1259

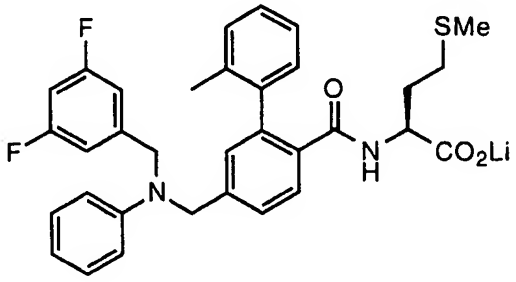
N-[4-*N*-(*N*-phenyl-*N*-(3,5-difluorobenzyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine lithium salt



Example 1259A

N-[4-*N*-(*N*-phenyl-*N*-(3,5-difluorobenzyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine, methyl ester

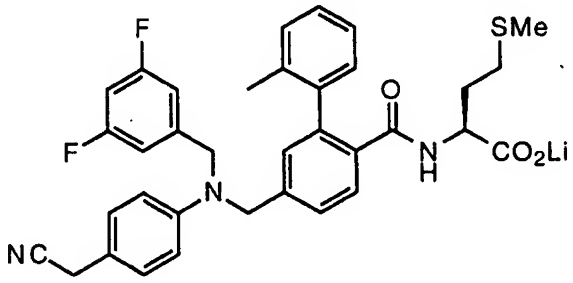
Prepared according to the procedure of example 1236A from reaction between 1236C and 3,5-difluorobenzyl bromide. NMR($CDCl_3$) 7.85-7.95 (m, 1H); 7.18-7.40 (m, 9H); 7.1 (s, 1H); 6.75-6.8 (m, 2H); 6.65-6.75 (m, 2H); 5.8-5.9 (m, 1H); 4.7 (s, 2H); 4.6 (m, 3H); 3.68 (s, 3H); 2.0-2.15 (m, 8H); 1.7-2.0 (m, 1H); 1.5-1.7 (m, 1H). (DSI/NH_3)/MS: 589$(M+H)^+$.



Example 1259B

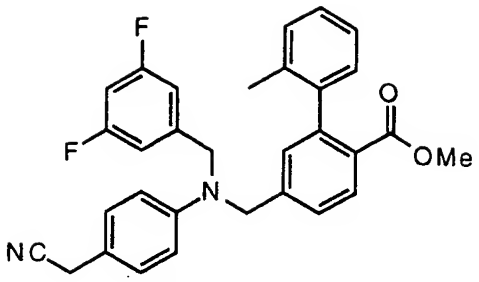
N-[4-*N*-(*N*-phenyl-*N*-(3,5-difluorobenzyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine lithium salt

Prepared according to the procedure of example 1178J from 1259A. NMR ^1H(MeOH-d_4): 7.7-7.8 (1H, m); 7.3-7.4 (1H, d), 7.0-7.3 (7H, d); 6.8-6.9 (3H, m); 6.6-6.8 (4H, m); 4.88 (2H, s); 4.85 (2H, s); 4.1-4.22 (1H, m); 1.7-2.1 (10H, m). ESI(-)/MS: 573(M-Li).



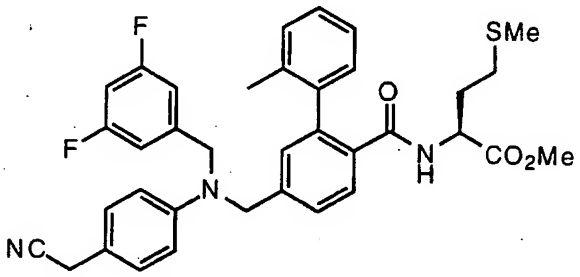
Example 1260

N-[4-*N*-(*N*-(4-acetonitrilephenyl-*N*-(3,5-difluorobenzyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine lithium salt.



Example 1260A

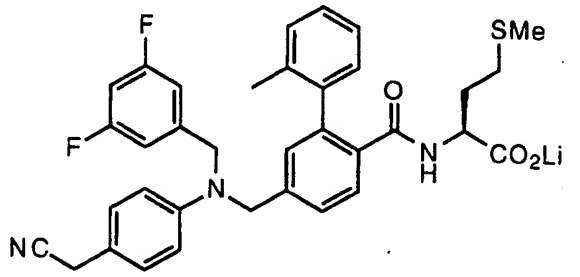
Prepared according to the procedure of example 1236A from reaction 3,5-difluorobenzyl bromide, 4-bromomethyl-2-)2-methylphenyl)benzoic methyl ester, and 4-aminobenzyl cyanide. NMR($CDCl_3$) 7.95-8.00 (m, 1H); 7.02-7.35 (m, 8H); 6.62-6.80 (m, 5H); 4.75 (s, 2H); 4.65 (s, 2H); 3.65 (s, 2H); 3.60 (s, 3H); 2.01 (s, 3H). (DSI/NH_3)/MS: 497$(M+H)^+$; 514$(M+NH_4)^+$.



Example 1260B

N-[4-*N*-(*N*-(4-acetonitrilephenyl-*N*-(3,5-difluorobenzyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine, methyl ester

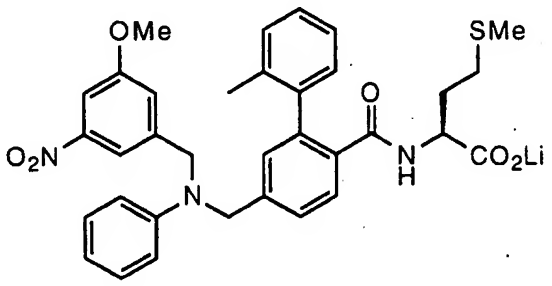
Prepared according to the procedure of example 1258C from example 1260A. NMR($CDCl_3$) 7.85-7.95 (m, 1H); 7.05-7.38 (m, 7H); 7.05 (s, 1H); 6.6-6.80 (m, 5H); 5.80-5.90 (m, 1H); 4.70 (s, 2H); 4.60 (s, 2H); 3.65 (s, 2H); 3.61 (s, 3H); 2.0-2.15 (m, 8H); 1.7-2.0 (m, 1H); 1.5-1.7 (m, 1H). (DSI/NH_3)/MS: 628$(M+H)^+$; 645$(M+NH_4)^+$.



Example 1260C

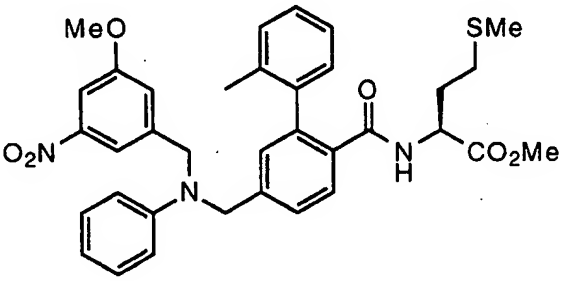
N-[4-*N*-(*N*-(4-acetonitrilephenyl-*N*-(3,5-difluorobenzyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine lithium salt.

Prepared according to the procedure of example 1178J from example 1260B. NMR ^{1}H(MeOH-d4): 7.6-7.7 (1H, m); 7.3-7.4 (1H, m), 7.0-7.3 (8H, m); 6.65-6.9 (5H, m); 4.78 (2H, s); 4.7 (3H, s); 4.1-4.22 (1H, m); 3.7 (2H, s); 1.7-2.1 (10H, m). ESI(-)/MS: 612(M-Li). Anal. Calcd for $C_{35}H_{32}F_2N_3O_3SLi \cdot 1.64\ H_2O$: C, 64.76; H, 5.48; N, 6.47. Found: C, 64.75; H, 5.19; N, 6.16.



Example 1261

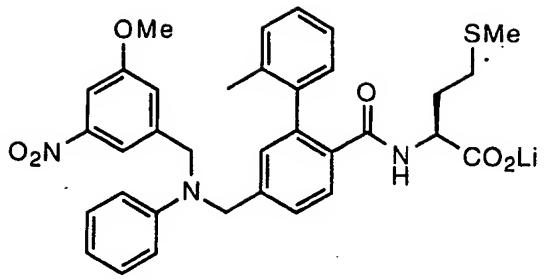
N-[4-*N*-(*N*-phenyl-*N*-(3-methoxy-5-nitrobenzyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine lithium salt.



Example 1261A

N-[4-*N*-(*N*-phenyl-*N*-(3-methoxy-5-nitrobenzyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine, methyl ester

Prepared according to the procedure of example 1236A from reaction between 1236C and 3-methoxy-5nitrobenzyl bromide. NMR($CDCl_3$) 8.1-8.2 (m, 2H); 8.0 (s, 1H); 7.68-7.95 (m, 1H); 7.1-7.40 (m, 8H); 6.9-6.95 (m, 1H); 6.7-6.8 (m, 1H); 6.6-6.7 (m, 2H); 5.8-5.9 (m, 1H); 4.78 (s, 2H); 4.6 (m, 3H); 3.92 (s, 3H); 3:68 (s, 3H); 2.0-2.15 (m, 8H); 1.7-2.0 (m, 1H); 1.5-1.7 (m, 1H). (DSI/NH_3)/MS: 628$(M+H)^+$.



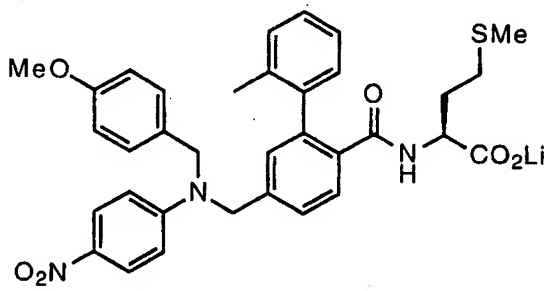
16005

Example 1261B

N-[4-*N*-(*N*-phenyl-*N*-(3-methoxy-5-nitrobenzyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine lithium salt.

Prepared according to the procedure of example 1178J from 1261A. NMR

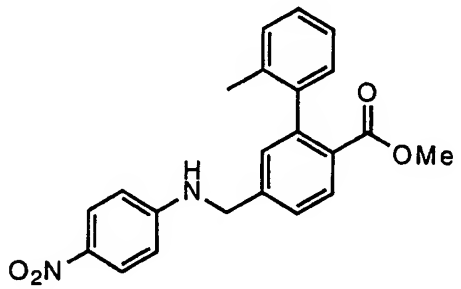
16010 ^{1}H(MeOH-d4): 8.1-8.2 (1H, m); 7.9-8.0 (1H, m), 7.6-7.7 (1H, m); 7.3-7.4 (1H, m); 7.0-7.3 (9H, m); 6.6-6.75 (3H, m); 4.8(2H, s); 4.72 (2H, s); 4.1-4.22(1H, m); 3.95 (3H, s); 1.7-2.1 (10H, m). ESI(-)/MS: 612(M-Li).



16015

Example 1262

N-[4-*N*-(*N*-(4-nitrophenyl-*N*-(4-methoxybenzyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine lithium salt.

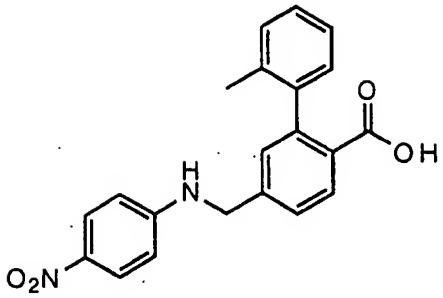


16020

Example 1262A

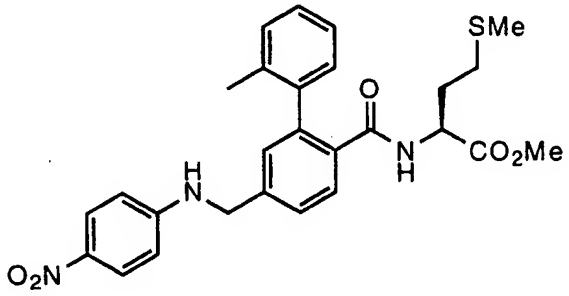
Prepared according to the procedure of example 1236A. Instead of using aniline, 4-nitroaniline was used to make the title compound. NMR($CDCl_3$) 8.08-8.11 (m, 2H); 7.94-8.00 (m, 1H); 7.38-7.42 (m, 1H); 7.18-7.24 (m, 5H); 7.0-7.18 (m, 1H); 6.55-6.60 (m,

2H); 4.95 (m, 1H); 4.52 (s, 2H); 3.60 (s, 3H); 2.00 (s, 3H). (DSI/NH_3)/MS: 394$(M+NH_4)^+$.



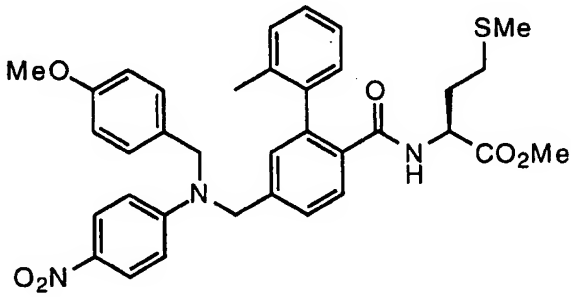
Example 1262B

Prepared according to the procedure of example 1178H from 1262A. NMR($CDCl_3$) 8.08-8.11 (m, 2H); 7.94-8.00 (m, 1H); 7.38-7.42 (m, 1H); 7.18-7.24 (m, 5H); 7.0-7.18 (m, 1H); 6.55-6.60 (m, 2H); 4.95 (m, 1H); 4.52 (s, 2H); 2.00 (s, 3H). (DSI/NH_3)/MS: 380$(M+NH_4)^+$.



Example 1262C

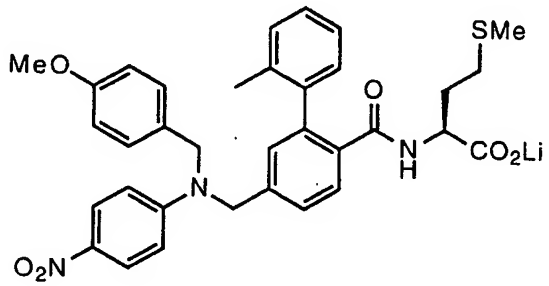
Prepared according to the procedure of example 1178I from 1262B. NMR($CDCl_3$) 8.08-8.11 (m, 2H); 7.94-8.00 (m, 1H); 7.38-7.42 (m, 1H); 7.20-7.38 (m, 5H); 7.18-7.20 (m, 1H); 6.55-6.60 (m, 2H); 5.89-5.95 (m, 1H); 4.95-5.00(m, 1H); 4.58-4.70 (m, 1H); 4.55 (m, 2H); 3.62 (s, 3H); 2.0-2.15 (m, 8H); 1.7-2.0 (m, 1H); 1.5-1.7 (m, 1H). (DSI/NH_3)/MS: 508$(M+H)^+$; 525$(M+NH_4)^+$.



Example 1262D

16045 *N*-[4-*N*-(*N*-(4-nitrophenyl-*N*-(4-methoxybenzyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine, methyl ester

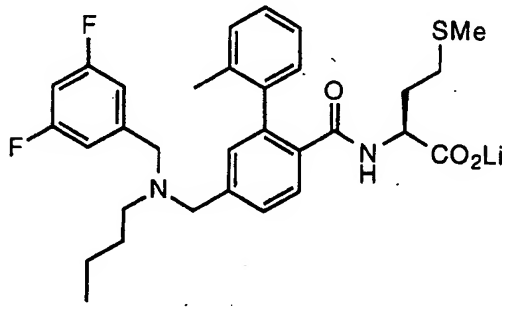
Prepared according to the procedure of example 1236A from reaction between 1262C and 4-methoxybenzyl bromide. NMR($CDCl_3$) 8.08-8.11 (m, 2H); 7.94-8.00 (m, 1H); 7.38-7.42 (m, 1H); 7.11-7.40 (m, 6H); 7.00 (m, 1H); 6.85-6.95 (m, 3H); 6.55-6.60 16050 (m, 2H); 5.89-5.95 (m, 1H); 4.80 (s, 2H); 4.70(s, 2H); 4.60-4.70 (m, 1H); 3.80 (s, 3H); 3.67 (s, 3H); 2.0-2.15 (m, 8H); 1.7-2.0 (m, 1H); 1.5-1.7 (m, 1H). (DSI/NH_3)/MS: 628$(M+H)^+$.



16055 Example 1262E

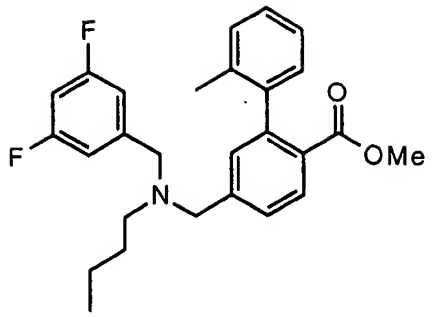
N-[4-*N*-(*N*-(4-nitrophenyl-*N*-(4-methoxybenzyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine lithium salt.

Prepared according to the procedure of example 1178J from 1262D. NMR ^1H(MeOH-d4): 8.0-8.05 (2H, m); 7.4-7.5 (1H, m), 7.3-7.4 (1H, m); 7.18-7.3 (7H, m); 16060 7.0 (1H, m); 6.8-6.9 (4H, m); 4.8-4.85 (4H, m); 4.1-4.22 (1H, m); 3.88 (3H, s); 1.7-2.1 (10H, m). ESI(-)/MS: 612(M-Li).



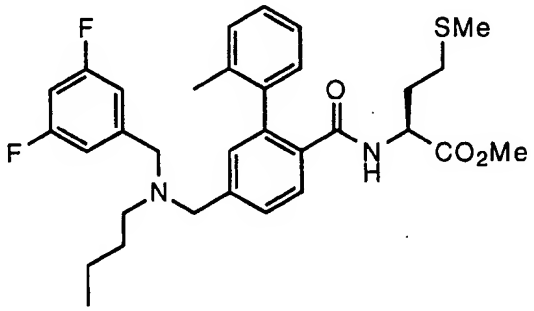
16065 Example 1263

N-[4-*N*-(*N*-butyl-*N*-(3,5-difluorobenzyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine lithium salt.



Example 1263A

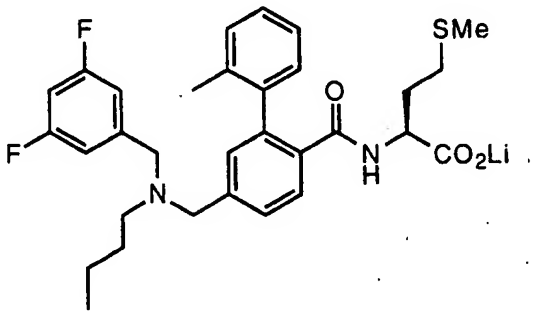
Prepared according to the procedure of example 1258A from reaction between 1258A and butyraldehyde. NMR($CDCl_3$) 7.92-7.98 (m, 1H); 7.38-7.45 (m, 1H); 7.10-7.32 (m, 4H); 7.0-7.1 (m, 1H); 6.8-6.95 (m, 2H); 6.60-6.75 (m, 1H); 3.58-3.63 (m, 5H); 3.55 (s, 2H); 2.38-2.48 (t, 2H); 2.07 (s, 3H); 1.4-1.6 (m, 2H); 1.2-1.4 (m, 2H); 0.8-0.9 (t, 3H). (DSI/NH_3)/MS: 437$(M+H)^+$.



Example 1263B

N-[4-*N*-(*N*-butyl-*N*-(3,5-difluorobenzyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine, methyl ester

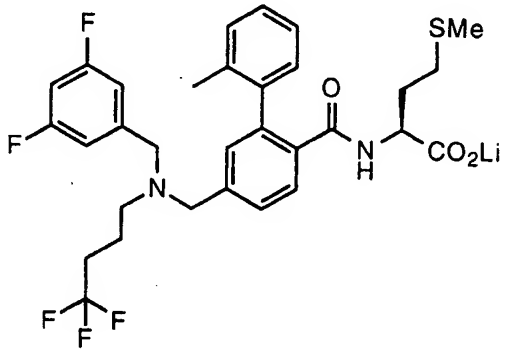
Prepared according to the procedure of example 1258C from 1263A. NMR($CDCl_3$) 7.9-8.00 (m, 1H); 7.40-7.46 (m, 1H); 7.20-7.40 (m, 4H); 7.20 (s, 1H); 6.7-6.85 (m, 2H); 6.60-6.75 (m, 1H); 5.82-5.92 (m, 1H); 4.58-4.70 (m, 1H); 3.65 (s, 3H); 3.60 (s, 2H); 3.55 (s, 2H); 2.40-2.48 (t, 2H); 2.20 (s, 3H); 1.8-1.96(m, 1H); 1.55-1.65 (m, 1H); 1.45-1.55 (m, 2H); 1.2-1.4 (m, 2H); 0.8-0.9 (t, 3H). (DSI/NH_3)/MS: 569$(M+H)^+$.



Example 1263C

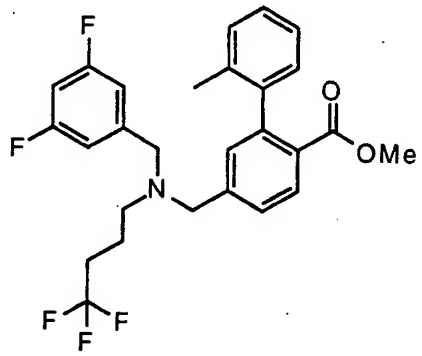
N-[4-*N*-(*N*-butyl-*N*-(3,5-difluorobenzyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine lithium salt.

Prepared according to the procedure of example 1178J from 1263B. NMR ^{1}H(MeOH-d4): 7.6-7.7 (1H, m); 7.4-7.48 (1H, m), 7.0-7.28 (6H, m); 6.9-7.0 (2H, m); 6.7-6.8 (1H, m); 4.1-4.22 (1H, m); 3.65 (2H, s); 3.58 (2H, s); 2.4-2.5 (2H, m); 2.21 (1H, m); 1.8-2.1 (10H, m); 1.4-1.5 (2H, m); 1.22-1.4 (2H, m); 0.8-0.9 (3H, m). ESI(-)/MS: 553(M-Li). Anal. Calcd for $C_{31}H_{35}F_2N_2O_3SLi \cdot 1.5\ LiOH \cdot 0.26H_2O$: C, 62.04; H, 6.05; N, 4.48. Found: C, 62.04; H, 6.05; N, 4.67.



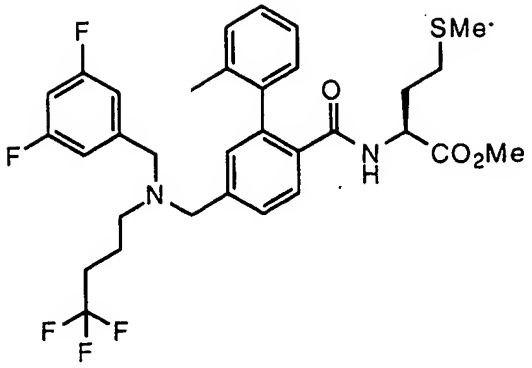
Example 1264

N-[4-*N*-(*N*-(4,4,4-trifluorobutyl-*N*-(3,5-difluorobenzyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine lithium salt.



Example 1264A

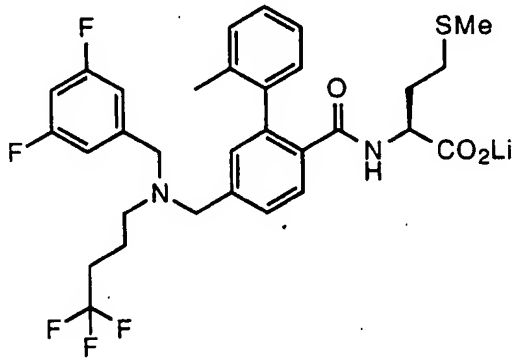
Prepared according to the procedure of example 1258A from reaction between 1258A and 4,4,4-trifluorobutyraldehyde. NMR($CDCl_3$) 7.92-7.98 (m, 1H); 7.38-7.45 (m, 1H); 7.10-7.32 (m, 4H); 7.0-7.1 (m, 1H); 6.8-6.92 (m, 2H); 6.62-6.78 (m, 1H); 3.58-3.63 (m, 5H); 3.55 (s, 2H); 2.43-2.55 (t, 2H); 2.00-2.1 (m, 5H); 1.7-1.82 (m, 2H).(DSI/NH_3)/MS: 492$(M+H)^+$.



Example 1264B

N-[4-*N*-(*N*-(4,4,4-trifluorobutyl-*N*-(3,5-difluorobenzyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine, methyl ester

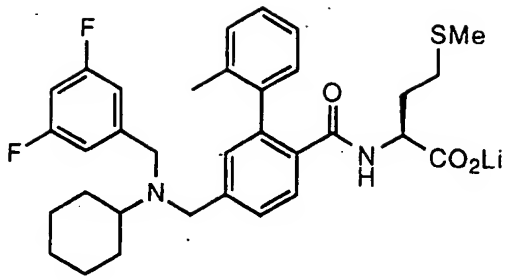
Prepared according to the procedure of example 1258C from 1264A. NMR($CDCl_3$) 7.9-8.00 (m, 1H); 7.40-7.46 (m, 1H); 7.20-7.40 (m, 4H); 7.20 (s, 1H); 6.7-6.85 (m, 2H); 6.60-6.75 (m, 1H); 5.82-5.92 (m, 1H); 4.58-4.70 (m, 1H); 3.65 (s, 3H); 3.61 (s, 2H); 3.55 (s, 2H); 2.40-2.48 (t, 2H); 1.5-2.16 (m, 14H). (DSI/NH_3)/MS: 623$(M+H)^+$.



Example 1264C

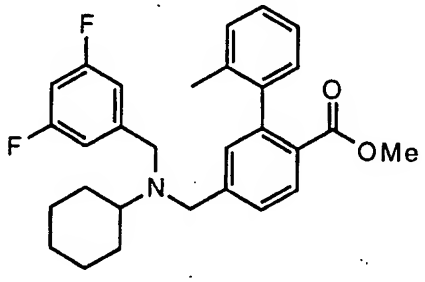
N-[4-*N*-(*N*-(4,4,4-trifluorobutyl-*N*-(3,5-difluorobenzyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine lithium salt.

Prepared according to the procedure of example 1178J from 1264B. NMR ^1H(MeOH-d4): 7.6-7.7 (1H, m); 7.4-7.48 (1H, m), 7.0-7.28 (6H, m); 6.9-7.0 (2H, m); 6.7-6.8 (1H, m); 4.1-4.22 (1H, m); 3.65 (2H, s); 3.6 (2H, s); 2.5-2.6 (2H, m); 1.6-2.25 (14H, m); 1.4-1.5 (2H, m); 1.22-1.4 (2H, m); 0.8-0.9 (3H, m). ESI(-)/MS: 609(M-Li). Anal. Calcd for $C_{31}H_{30}F_5N_2O_3SLi \cdot 1.21H_2O$: C, 58.70; H, 5.15; N, 4.42. Found: C, 58.69; H, 5.16; N, 4.18.



Example 1265

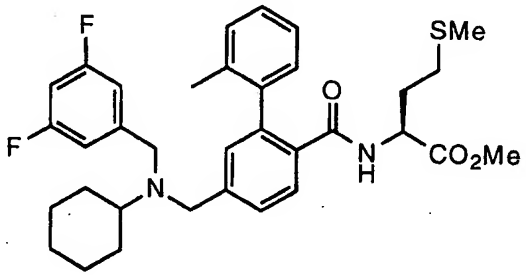
16135 *N*-[4-*N*-(*N*-cyclohexyl-*N*-(3,5-difluorobenzyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine lithium salt.



Example 1265A.

16140 Prepared according to the procedure of example 1258A from reaction between 1258A and cyclohexanone. NMR ($CDCl_3$) 7.90-7.95 (m, 1H); 7.40-7.45 (m, 1H); 7.18-7.38 (m, 4H); 7.00-7.09 (m, 1H); 6.84-6.94 (m, 2H); 6.58-6.68 (m, 1H); 3.68 (s, 2H); 3.62 (m, 5H); 2.40-2.50 (m, 1H); 2.08 (s, 3H); 1.75-1.96 (m, 4H); 1.05-1.65 (m, 6H). (DSI/NH_3)/MS: 464$(M+H)^+$.

16145



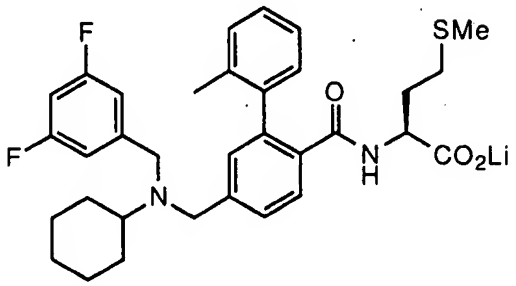
Example 1265B

N-[4-*N*-(*N*-cyclohexyl-*N*-(3,5-difluorobenzyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine, methyl ester

16150 Prepared according to the procedure of example 1258C from 1265A. NMR ($CDCl_3$) 7.85-7.95 (m, 1H); 7.38-7.45 (m, 1H); 7.18-7.38 (m, 4H); 7.2 (s, 1H); 6.84-6.94 (m, 2H); 6.58-6.68 (m, 1H); 5.85-5.93 (m, 1H); 4.56-4.65 (m, 1H); 3.70 (s, 2H); 3.65 (s,

2H); 3.61 (s, 3H); 2.40-2.50 (m, 1H); 1.96-2.18 (m, 7H); 1.71-1.96 (m, 6H); 1.55-1.68 (m ,1H); 1.05-1.52 (m, 6H). (DSI/NH_3)/MS: 595$(M+H)^+$.

16155

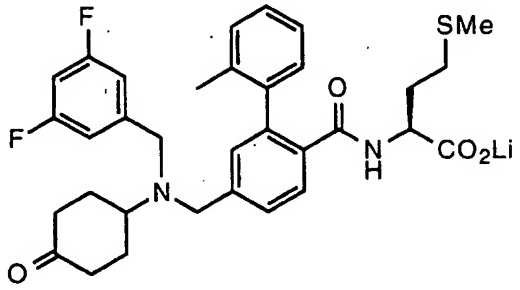


Example 1265C

N-[4-*N*-(*N*-cyclohexyl-*N*-(3,5-difluorobenzyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine lithium salt.

16160 Prepared according to the procedure of example 1178J from 1265B. NMR ^1H(MeOH-d_4): 7.6-7.7 (1H, m); 7.35-7.45 (1H, m), 7.0-7.35 (5H, m); 6.9-7.0 (2H, m); 6.7-6.8 (1H, m); 4.1-4.22 (1H, m); 3.7 (3H, s); 3.65 (3H, s); 2.4-2.52 (1H, m); 2.1 (1H, m); 1.7-2.1 (11H, m); 1.5-1.7 (2H, m); 1.23-1.5 (2H, m); 1.05-1.25 (3H, m). ESI(-)/MS: 579(M-Li).

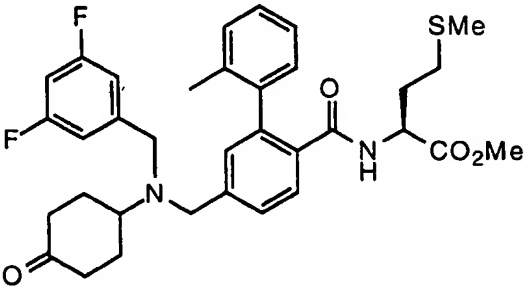
16165



Example 1266

N-[4-*N*-(*N*-(4-cyclohexanonyl)-*N*-(3,5-difluorobenzyl)aminomethyl)-2-(2-

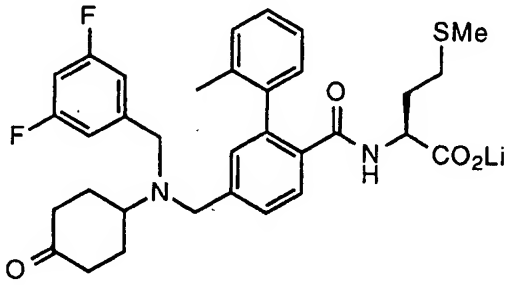
16170 methylphenyl)benzoyl]methionine lithium salt.



Example 1266A

N-[4-*N*-(*N*-(4-cyclohexanonyl)-*N*-(3,5-difluorobenzyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine, methyl ester

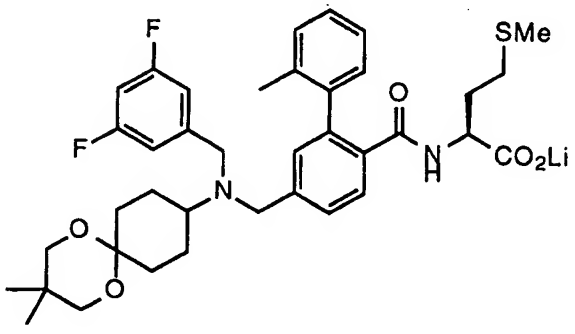
A mixture of 1267B (0.42 g, 0.604 mmol) and 10 ml of 10% of HCl in 35 ml of acetone was refluxed until all 1267B disappeared. Solvents were removed under vacuum. The residue was treated with 20 ml of 2N Na_2CO_3, then extracted by 50 ml of EtOAc. The organic solution was then washed with brine, dried over anhydrous $MgSO_4$. The crude product was purified by flash chromatography eluting with 1:1 EtOAc/Hexane to afforded 0.25 g of the title compound. NMR ($CDCl_3$) 7.82-7.95 (m, 1H); 7.40-7.49 (m, 1H); 7.18-7.40 (m, 5H); 6.82-6.92 (m, 2H); 6.58-6.68 (m, 1H); 5.82-5.91 (m, 1H); 4.58-4.68 (m, 1H); 3.61-3.75 (m, 7H); 2.95-3.05 (m, 1H); 1.5-2.5 (m, 18H). (DSI/NH3)/MS: 609$(M+H)^+$; 626$(M+NH4)^+$.



Example 1266B

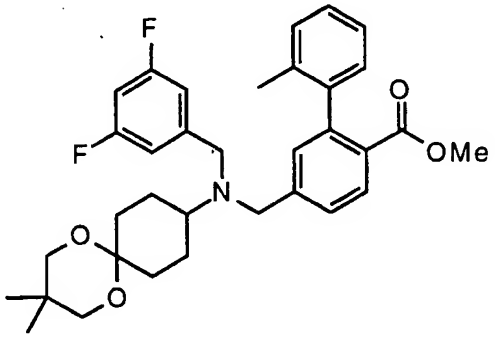
N-[4-*N*-(*N*-(4-cyclohexanonyl)-*N*-(3,5-difluorobenzyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine lithium salt.

Prepared according to the procedure of example 1178J from 1266A. NMR ^1H(MeOH-d_4): 7.6-7.7 (1H, m); 7.4-7.5 (1H, m), 7.0-7.28 (6H, m); 6.9-7.0 (2H, m); 6.7-6.8 (1H, m); 4.1-4.22 (1H, m); 3.75 (2H, s); 3.7 (2H, s); 2.1-2.3 (3H, m); 1.76-2.1 (14H, m); 1.5-1.78 (2H, m). ESI(-)/MS: 593(M-Li). Anal. Calcd for $C_{33}H_{35}F_2N_2O_4SLi \cdot 1.73H_2O \cdot 1.5LiOH$: C, 60.32; H, 5.95; N, 4.26. Found: C, 60.33; H, 5.62; N, 4.04.



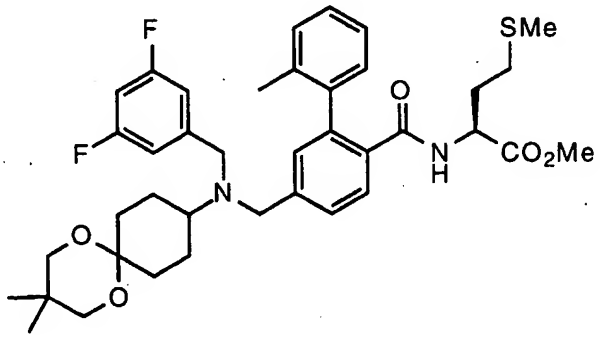
Example 1267

N-[4-*N*-(*N*-(4-(2,2-dimethyltrimethylene ketal)-cyclohexyl)-*N*-(3,5-difluorobenzyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine lithium salt.



Example 1267A

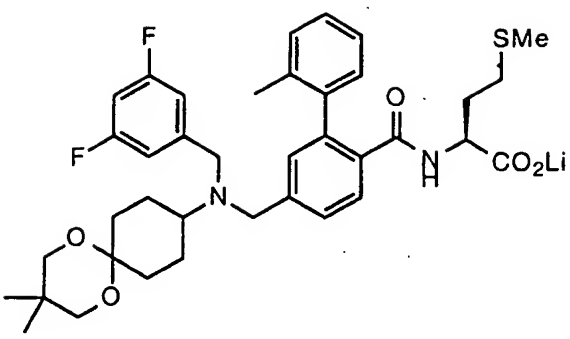
Prepared according to the procedure of example 1258A from reaction between 1258A and 1,4-cyclohexanedione *mono*-2,2-dimethyltrimethylene ketal. NMR ($CDCl_3$) 7.82-7.92 (m, 1H); 7.36-7.42 (m, 1H); 7.18-7.38 (m, 4H); 7.20 (s, 1H); 6.82-6.92 (m, 2H); 6.58-6.68 (m, 1H);3.68 (s, 2H); 3.60 (s, 3H); 3.59 (s, 2H); 3.48 (s, 2H); 3.42 (s, 2H); 2.50-2.60 (m, 1H); 2.22-2.38 (m, 2H); 1.80-2.20 (m, 6H); 1.2-1.3 (m, 2H); 0.95 (s, 6H). (DSI/NH3)/MS: 564$(M+H)^+$.



Example 1267B

N-[4-*N*-(*N*-(4-(2,2-dimethyltrimethylene ketal)-cyclohexyl)-*N*-(3,5-difluorobenzyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine, methyl ester

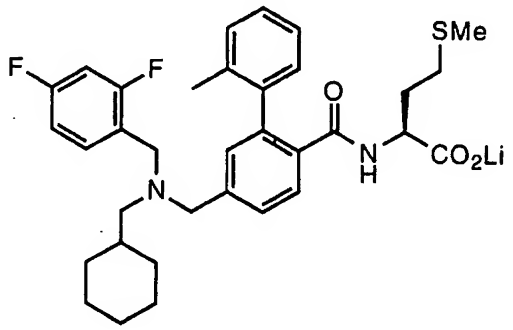
Prepared according to the procedure of example 1258C from 1267A. NMR ($CDCl_3$) 7.82-7.92 (m, 1H); 7.36-7.42 (m, 1H); 7.18-7.38 (m, 4H); 7.20 (s, 1H); 6.82-6.92 (m, 2H); 6.58-6.68 (m, 1H); 5.82-5.91 (m, 1H); 4.58-4.68 (m, 1H); 3.68 (s, 2H); 3.60 (s, 3H); 3.59 (s, 2H); 3.48 (s, 2H); 3.42 (s, 2H); 2.50-2.60 (m, 1H); 2.22-2.38 (m, 2H); 1.50-2.2 (m, 14H); 1.2-1.3 (m, 2H); 0.95 (s, 6H). (DSI/NH3)/MS: 695$(M+H)^+$.



Example 1267C

16225 *N*-[4-*N*-(*N*-(4-(2,2-dimethyltrimethylene ketal)-cyclohexyl)-*N*-(3,5-difluorobenzyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine lithium salt.

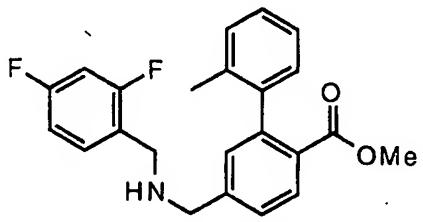
Prepared according to the procedure of example 1178J from 1267B. NMR ^{1}H(MeOH-d4): 7.55-7.65 (1H, m); 7.38-7.48 (1H, m), 7.0-7.35 (6H, m); 6.9-7.0 (2H, m); 6.7-6.8 (1H, m); 4.1-4.22 (1H, m); 3.7 (2H, s); 3.65(2H, s); 3.45 (4H, s); 2.5-2.65 16230 (1H, m); 2.26-2.4 (2H, m); 2.2 (1H, s); 1.5-2.1 (13H, m); 1.1-1.3 (2H, m); 0.95 (6H, s). ESI(-)/MS: 686.79(M-Li). Anal. Calcd for $C_{38}H_{45}F_2N_2O_5SLi \cdot 0.99H_2O \cdot 1.0LiOH$: C, 62.65; H, 6.64; N, 3.84. Found: C, 62.65; H, 6.33; N, 3.71.



16235

Example 1268

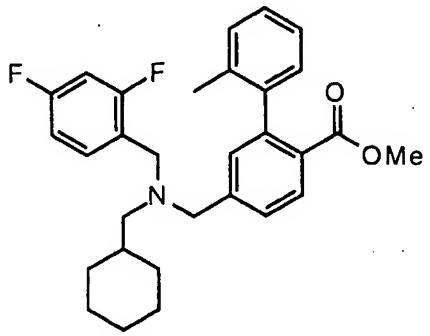
N-[4-*N*-(*N*-cyclohexylmethyl-*N*-(2,4-difluorobenzyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine lithium salt.



16240

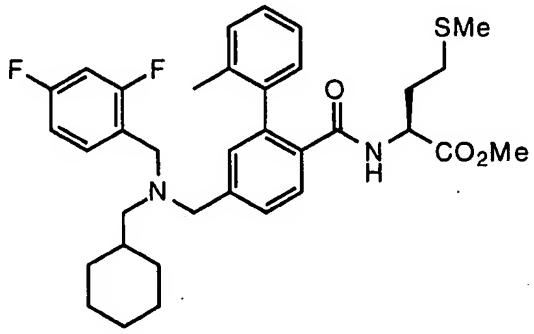
Example 1268A

Prepared according to the procedure of example 1258A from the reaction between 2,4-difluorobenzyl amine and 4-formyl-2-(2-methylphenyl)benzoic acid methyl ester. NMR ($CDCl_3$) 7.22-7.30 (m, 2H); 6.85-6.90 (m, 3H); 3.88 (s, 2H); 2.40-2.45 (m, 2H); 1.6-1.8 (m, 5H); 1.38-1.60 (m, 2H); 1.05-1.40 (m, 3H); 0.8-1.0 (m, 2H). (DSI/NH3)/MS: 240$(M+H)^+$.



Example 1268B

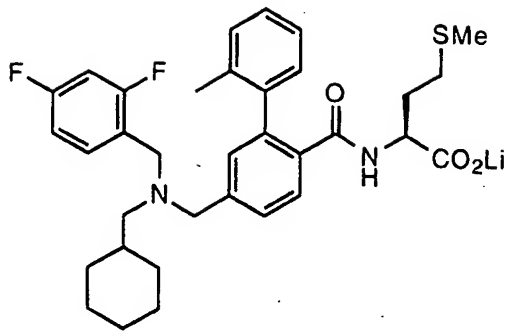
Prepared according to the procedure of example 1258A from reaction between 1268A and cyclohexanecarboxaldehyde. NMR ($CDCl_3$) 7.90-7.95 (m, 1H); 7.38-7.47 (m, 2H); 7.20-7.35 (m, 4H); 7.0-7.10 (m, 1H); 6.75-6.85 (m, 2H); 3.60(s, 3H); 3.55 (s, 2H); 3.52 (s, 2H); 2.20-2.23 (m, 2H); 2.05 (s, 3H); 1.72-1.83 (m, 2H); 1.52-1.72 (m, 4H); 1.10-1.30 (m, 3H); 0.6-0.8 (m, 2H). (DSI/NH3)/MS: 478$(M+H)^+$.



Example 1268C

N-[4-*N*-(*N*-cyclohexylmethyl-*N*-(2,4-difluorobenzyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine, methyl ester

Prepared according to the procedure of example 1258C from 1268B. NMR ($CDCl_3$) 7.85-7.95 (m, 1H); 7.20-7.47 (m, 6H); 7.18 (s, 1H); 6.75-6.85 (m, 2H); 5.85-5.92 (m, 1H); 4.56-4.67 (m, 1H); 3.67(s, 3H); 3.57 (s, 2H); 3.55 (s, 2H); 2.18-2.23 (m, 4H); 2.00-2.11 (m, 6H); 1.72-1.83 (m, 3H); 1.52-1.72 (m, 4H); 1.10-1.30 (m, 3H); 0.6-0.8 (m, 2H). (DSI/NH3)/MS: 609$(M+H)^+$.

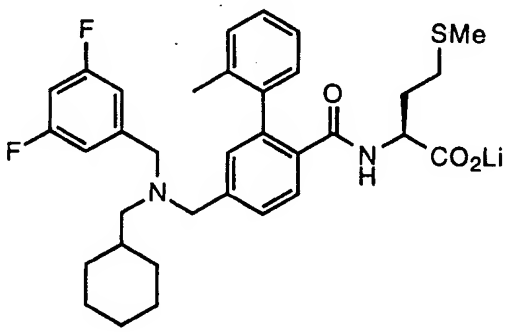


Example 1268D

N-[4-*N*-(*N*-cyclohexylmethyl-*N*-(2,4-difluorobenzyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine lithium salt.

16270 Prepared according to the procedure of example 1178J from 1267C. NMR ^{1}H(MeOH-d4): 7.6-7.7 (1H, m); 7.38-7.48 (2H, m), 7.0-7.28 (6H, m); 6.8-6.95 (2H, m); 4.1-4.22 (1H, m); 4.58 (4H, s); 2.2-2.3 (4H, m); 1.76-2.1 (9H, m); 1.5-1.78 (5H, m); 1.1-1.3 (3H, m); 0.7-0.82 (2H, m). ESI(-)/MS: 593(M-Li).

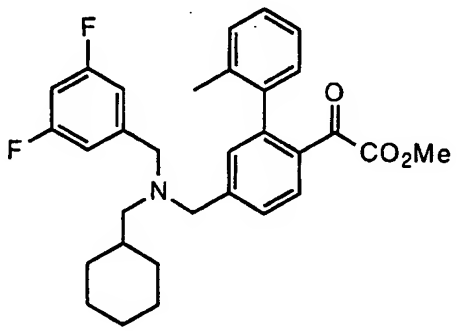
16275



Example 1269

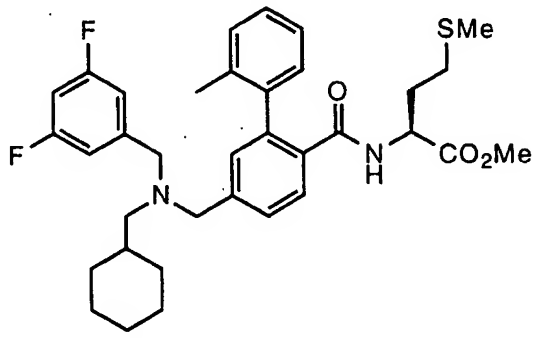
N-[4-*N*-(*N*-cyclohexylmethyl-*N*-(3,5-difluorobenzyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine lithium salt.

16280



Example 1269A

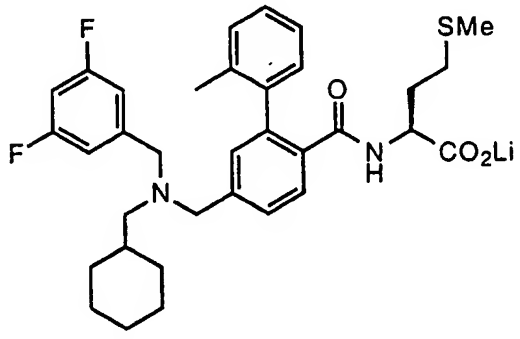
Prepared according to the procedure of example 1258A from reaction between 1258A and cyclohexanecarboxaldehyde. NMR ($CDCl_3$) 7.95-8.05 (m, 1H); 7.40-7.47 (m, 1H); 7.15-7.35 (m, 5H); 7.04-7.11 (m, 1H); 6.75-6.85 (m, 2H); 6.60-6.70 (m, 1H); 3.60(s, 3H); 3.55 (s, 2H); 3.45 (s, 2H); 2.18-2.25 (m, 2H); 2.05 (s, 3H); 1.72-1.83 (m, 2H); 1.52-1.72 (m, 4H); 1.10-1.30 (m, 3H); 0.6-0.8 (m, 2H). (DSI/NH3)/MS: 478$(M+H)^+$.



Example 1269B

N-[4-*N*-(*N*-cyclohexylmethyl-*N*-(3,5-difluorobenzyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine, methyl ester

Prepared according to the procedure of example 1258C from 1269A. NMR ($CDCl_3$) 7.79-7.95 (m, 1H); 7.40 -7.48 (m, 1H); 7.20-7.41 (m, 5H); 7.18 (s, 1H); 6.75-6.85 (m, 2H); 6.60-6.70 (m, 1H); 5.85-5.92 (m, 1H); 4.56-4.67 (m, 1H); 3.67(s, 3H); 3.57 (s, 2H); 3.45 (s, 2H); 2.18-2.23 (m, 4H); 2.00-2.11 (m, 6H); 1.72-1.83 (m, 3H); 1.52-1.72 (m, 4H); 1.10-1.30 (m, 3H); 0.6-0.8 (m, 2H). (DSI/NH3)/MS: 609$(M+H)^+$.



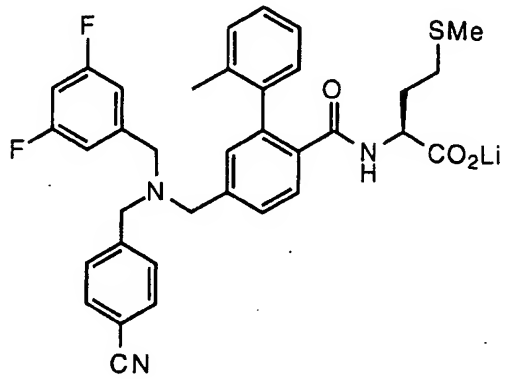
Example 1269C

N-[4-*N*-(*N*-cyclohexylmethyl-*N*-(3,5-difluorobenzyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine lithium salt.

Prepared according to the procedure of example 1178J from 1269B. NMR ^1H(MeOH-d4): 7.6-7.7 (1H, m); 7.38-7.48 (1H, m), 7.0-7.28 (6H, m); 6.9-7.0 (2H, m); 6.7-6.8 (1H, m); 4.1-4.22 (1H, m); 4.6 (2H, s); 4.55 (2H, s); 2.2-2.3 (4H, m); 1.76-2.1

(9H, m); 1.5-1.78 (5H, m); 1.1-1.3 (3H, m); 0.7-0.82 (2H, m). ESI(-)/MS: 593(M-Li). Anal. Calcd for $C_{31}H_{30}F_5N_2O_3SLi \cdot 1.0LiOH$: C, 65.38; H, 6.45; N, 4.48 Found: C, 65.43; H, 6.17; N, 4.40.

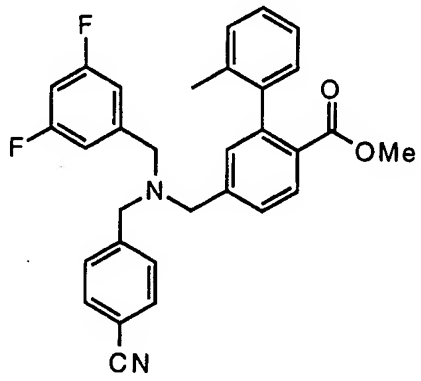
16310



Example 1270

N-[4-*N*-(*N*-(4-cyanobenzyl)-*N*-(3,5-difluorobenzyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine lithium salt.

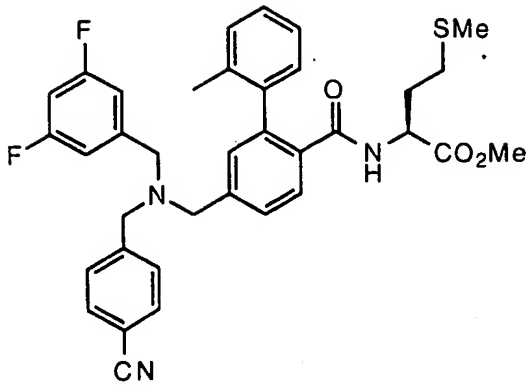
16315



Example 1270A

Prepared according to the procedure of example 1258A from reaction between 1258A and 4-cyanobenzaldehyde. NMR(CDCl3) 7.95-8.00 (m, 1H); 7.60-7.65 (m, 2H); 7.40-7.56 (m, 3H); 7.20-7.38 (m, 4H); 7.00-7.10 (m, 1H); 6.85-6.95 (m, 2H); 6.65-6.75 (, 1H); 3.58-3.65 (m, 7H); 3.54-3.58 (m, 2H); 2.05 (s, 3H). (DSI/NH3)/MS: 585(M+H)+ ; 497 (M+NH4)+. 514 (M+NH4)+.

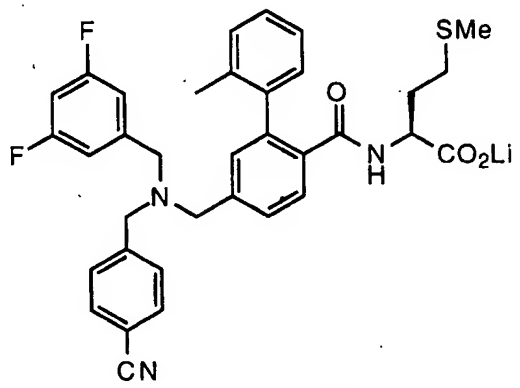
16320



Example 1270B

N-[4-*N*-(*N*-(4-cyanobenzyl)-*N*-(3,5-difluorobenzyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine, methyl ester

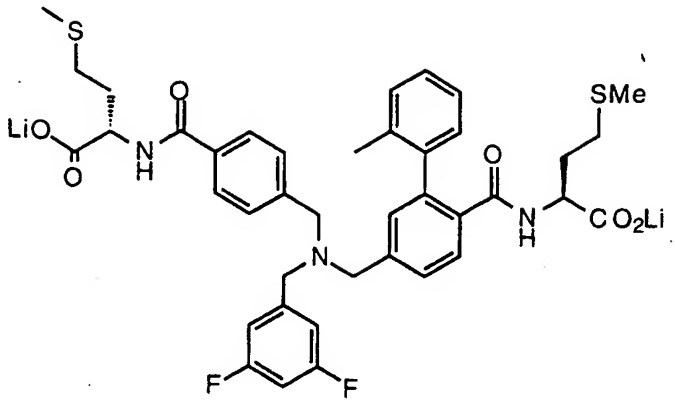
Prepared according to the procedure of example 1258C from 1270A. NMR($CDCl_3$) 8.00-8.18 (m, 1H); 7.76-7.80 (m, 2H); 7.48-7.76 (m, 3H); 7.10-7.38 (m, 5H); 7.00-7.11 (m, 2H); 6.80-6.85 (m, 1H); 5.95-6.05 (m, 1H); 4.70-4.81 (m, 1H); 3.70-3.90 (m, 9H); 3.54-3.58 (m, 2H); 1.95-2.20 (m, 8H); 1.7-2.0 (m, 1H); 1.5-1.7 (m, 1H). (DSI/NH3)/MS: 628$(M+H)^+$; 645$(M+NH4)^+$.



Example 1270C

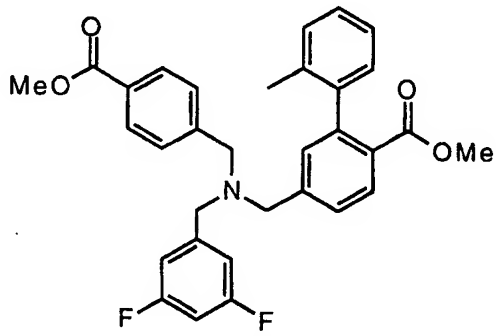
N-[4-*N*-(*N*-(4-cyanobenzyl)-*N*-(3,5-difluorobenzyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine lithium salt.

Prepared according to the procedure of example 1178J from 1270B. NMR ^1H(MeOH-d4): 8.78 (1H, s); 7.6-7.7 (2H, m); 7.5-7.6 (2H, m), 7.5-7.55 (1H, m); 7.0-7.3 (6H, m); 6.9-7.0 (2H, m); 6.77-6.82 (1H, m); 4.1-4.22 (1H, m); 3.7 (2H, s); 3.65 (2H, s,); 3.6 (2H, s); 1.5-2.2 (10H, m).ESI(-)/MS: 612(M-Li).



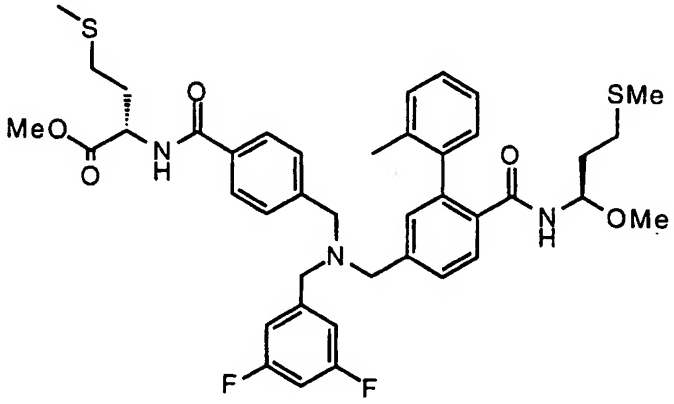
Example 1271

N-[4-*N*-(*N*-(3,5-difluorobenzyl)-*N*-(4-*N*-carboxymethionine)benzyl)aminomethyl-2-(2-methylphenyl)benzoyl]methionine dilithium salt.



Example 1271A

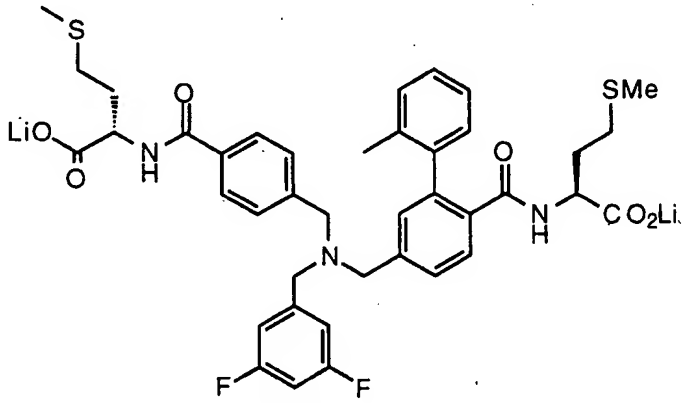
Prepared according to the procedure of example 1236A from reaction between 1258A and 4-bromomethyl-benzoic methyl ester. NMR($CDCl_3$) 7.75-7.90 (m, 1H); 7.75-7.85 (m, 2H); 7.40-7.50 (m, 2H); 7.20-7.40 (m, 5H); 7.18 (s, 1H); 6.88-6.95 (m, 2H); 6.70-6.80 (m, 1H); 585-5.95 (m, 1H); 4.58-4.70 (m, 1H); 3.80 (s, 3H); 3.65 (s, 3H); 3.60 (s, 2H); 3.55 (s, 2H).(DSI/NH3)/MS: 530$(M+H)^+$.



Example 1271B

N-[4-*N*-(*N*-(3,5-difluorobenzyl)-*N*-(4-*N*-carboxymethionine)benzyl)aminomethyl-2-(2-methylphenyl)benzoyl]methionine dimethyl ester.

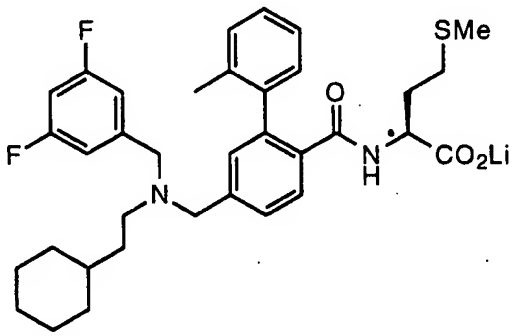
Prepared according to the procedure of example 1258C from 1271A. NMR($CDCl_3$) 7.75-7.90 (m, 1H); 7.75-7.85 (m, 2H); 7.40-7.50 (m, 2H); 7.20-7.40 (m, 5H); 7.18 (s, 1H); 6.88-6.95 (m, 3H); 6.70-6.80 (m, 1H); 5.85-5.95 (m, 1H); 4.90-4.95 (m, 1H); 4.58-4.70 (m, 1H); 3.80 (s, 3H); 3.65 (s, 3H); 3.60 (s, 2H); 3.55 (s, 2H); 2.58-2.70 (m, 2H); 2.0-2.15 (m, 10H); 1.7-2.0 (m, 3H); 1.5-1.7 (m, 2H). (DSI/NH3)/MS: 792$(M+H)^+$.



Example 1271C

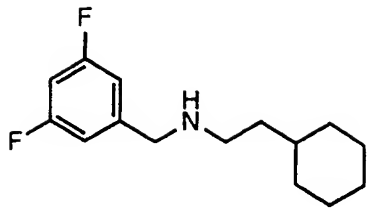
N-[4-*N*-(*N*-(3,5-difluorobenzyl)-*N*-(4-*N*-carboxymethionine)benzyl)aminomethyl-2-(2-methylphenyl)benzoyl]methionine dilithium salt.

Prepared according to the procedure of example 1178J from 1271B. NMR ^1H (d4-MeOH): 7.8-7.9 (2H, m); 7.6-7.7 (1H, m); 7.45-7.55 (4H, m); 7.1-7.3 (6H, m); 6.9-7.05 (2H, m); 6.75-6.85 (1H, m); 4.5-4.6 (1H, m); 4.2-4.3(1H, m); 3.4-3.5 (6H, m); 2.5-2.6 (2H, m); 1.5-2.3 (15H, m). ESI(-)/MS: 762 (M-Li); 764(M+H); 781(M+NH_4).



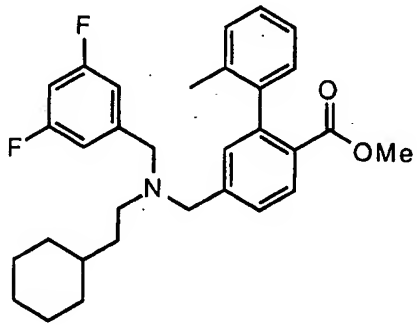
Example 1272

N-[4-*N*-(*N*-(2-cyclohexylethyl-*N*-(3,5-difluorobenzyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine lithium salt.



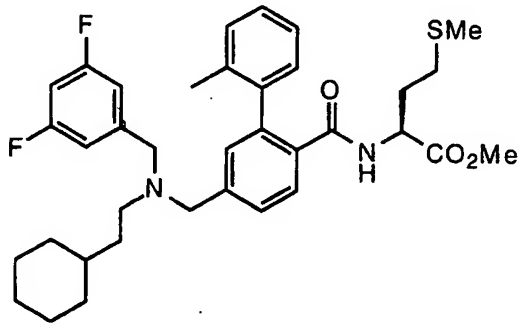
Example 1272A

Prepared according to the procedure of example 1258A from reaction between 3,5-difluorobenzaldehyde and 2-cyclohexyle-1-aminoethane. NMR($CDCl_3$) 6.78-6.95 (m, 2H); 6.65-6.80 (m, 3H); 3.78 (s, 2H); 2.58-2.68 (m, 2H); 1.00-1.75 (m, 11H); 0.8-1.0- (m, 2H). (DSI/NH3)/MS: 254$(M+H)^+$; 271$(M+NH4)^+$.



Example 1272B

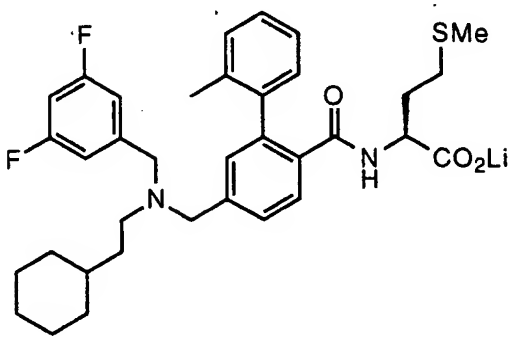
Prepared according to the procedure of example 1226A from the reaction between 1272A and 4-Bromomethyl-2-(2-methylphenyl)benzoic acid, methyl ester. NMR($CDCl_3$) 7.91-7.98 (m, 1H); 7.38-7.45 (m, 1H); 7.10-7.30 (m, 4H); 7.05-7.15 (m, 1H); 6.83-6.95 (m, 2H); 6.60-6.78 (m, 1H); 3.60 (s, 5H); 3.55 (s, 2H); 2.40-2.50 (m, 2H); 2.05 (s, 3H); 1.50-1.75 (m, 5H); 1.30-1.47 (m, 2H); 1.00-1.38 (m, 4H); 0.74-0.90 (m, 2H). (DSI/NH3)/MS: 492$(M+H)^+$.



Example 1272C

N-[4-*N*-(*N*-(2-cyclohexylethyl-*N*-(3,5-difluorobenzyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine, methyl ester

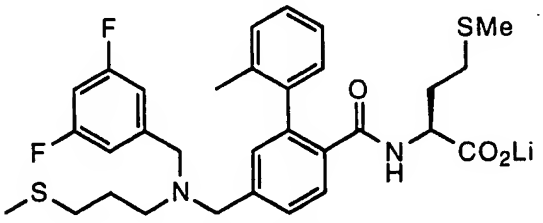
Prepared according to the procedure of example 1258C from 1272B. NMR(CDCl3) 7.81-7.98 (m, 1H); 7.38-7.45 (m, 2H); 7.20-7.40 (m, 3H); 7.18 (s, 1H); 6.83-6.95 (m, 2H); 6.60-6.78 (m, 1H); 5.81-5.90 (m, 1H); 4.58-4.70 (m, 1H); 3.67 (s, 3H); 3.60 (s, 2H); 3.55 (s, 2H); 2.40-2.50 (m, 2H); 2.00-2.20 (m, 8H); 1.70-2.00 (m, 1H); 1.50-1.70 (m, 5H); 1.30-1.50 (m, 2H); 1.10-1.38 (m, 4H); 0.74-0.90 (m, 2H). (DSI/NH3)/MS: 623(M+H)+ .



Example 1272D

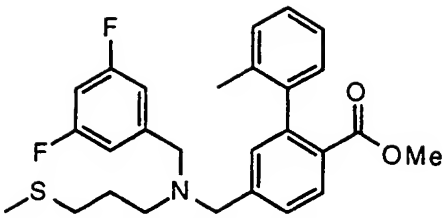
N-[4-*N*-(*N*-(2-cyclohexylethyl-*N*-(3,5-difluorobenzyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine lithium salt.

Prepared according to the procedure of example 1178J from 1272C. NMR ^{1}H(MeOH-d4): 7.6-7.7 (1H, m); 7.4-7.48 (1H, m), 7.0-7.28 (6H, m); 6.9-7.0 (2H, m); 6.7-6.8 (1H, m); 4.1-4.22 (1H, m); 3.65 (2H, s); 3.58 (2H, s); 2.4-2.5 (2H, m); 2.21 (1H, m); 1.1-2.1 (20H, m); 0.8-0.9 (2H, m). ESI(-)/MS: 607(M-Li).



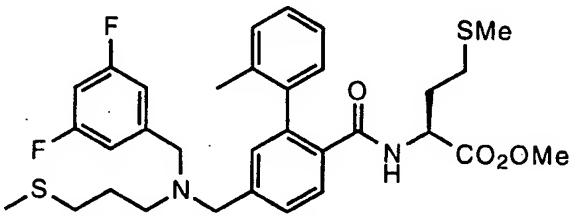
Example 1273

N-[4-*N*-(*N*-(3-methylthiopropyl)-*N*-(3,5-difluorobenzyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine lithium salt.



Example 1273A

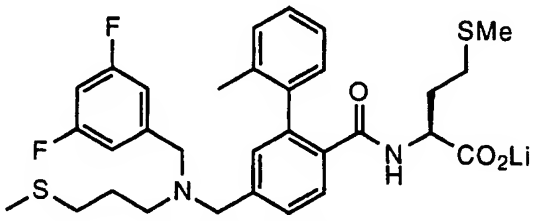
Prepared according to the procedure of example 1258A from reaction between 1258A and 3-(methylthio)propionaldehyde. NMR($CDCl_3$) 7.91-7.98 (m, 1H); 7.38-7.45 (m, 1H); 7.20-7.30 (m, 4H); 7.04-7.10 (m, 1H); 6.83-6.90 (m, 2H); 6.60-6.74 (m, 1H); 3.60 (s, 5H); 3.55 (s, 2H); 2.50-2.60 (t, 2H); 2.42-2.50 (t, 2H); 2.10 (s, 3H); 2.05 (s, 3H); 1.70-1.84 (m, 2H). (DSI/NH3)/MS: 470$(M+H)^+$.



Example 1273B

N-[4-*N*-(*N*-(3-methylthiopropyl)-*N*-(3,5-difluorobenzyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine, methyl ester

Prepared according to the procedure of example 1258C from 1273A. NMR($CDCl_3$) 7.81-7.98 (m, 1H); 7.38-7.45 (m, 2H); 7.20-7.40 (m, 3H); 7.18 (s, 1H); 6.83-6.95 (m, 2H); 6.60-6.78 (m, 1H); 5.81-5.90 (m, 1H); 4.58-4.70 (m, 1H); 3.67 (s, 3H); 3.63 (s, 2H); 3.55 (s, 2H); 2.50-2.60 (t, 2H); 2.42-2.50 (t, 2H); 1.92-2.20 (m, 9H); 1.65-1.95 (m, 4H); 1.5-1.65 (m, 2H). (DSI/NH3)/MS: 601$(M+H)^+$.

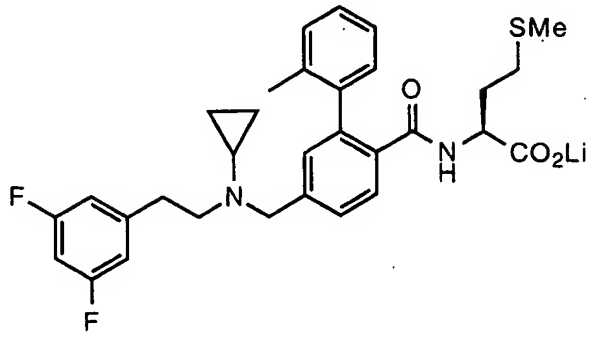


Example 1273C

N-[4-*N*-(*N*-(3-methylthiopropyl)-*N*-(3,5-difluorobenzyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine lithium salt.

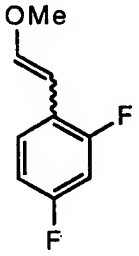
Prepared according to the procedure of example 1178J from 1273B. NMR ^1H(MeOH-d4): 7.6-7.7 (1H, m); 7.4-7.48 (1H, m), 7.0-7.3 (6H, m); 6.9-7.0 (2H, m);

6.7-6.8 (1H, m); 4.1-4.22 (1H, m); 4.65 (2H, s), 4.60 (2H, s); 2.5-2.6 (2H, m); 2.4-2.5 (2H, m); 1.8-2.3 (13H, m). ESI(-)/MS: 585(M-Li).



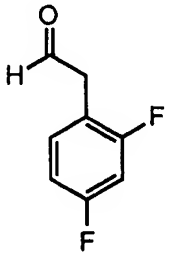
Example 1275

N-[4-*N*-(*N*-cyclopropyl-*N*-(2-(3,5-difluorophenyl)ethyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine lithium salt.



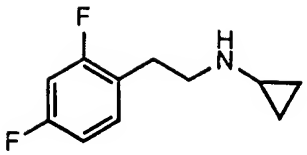
Example 1275A

Prepared according to the procedure of example 1279A from the reaction between 2,4-difluorobenzaldehyde and (Methoxymethyl)triphenylphosphonium chloride. NMR. 7.18-7.21 (m, 2H); 6.80-6.94 (m, 3H); 6.06 (s, 1H); 5.84 (s, 1H); 3.78 (s, 3H). DSI/NH_3)MS: 171$(M+H)^+$; 188$(M+NH_4)^+$.



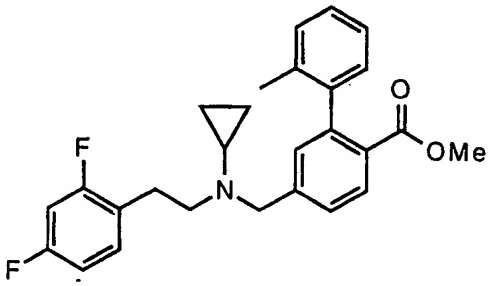
Example 1275B

Prepared according to the procedure of example 1279B from example 1275A. NMR. 9.78 (s, 1H); 7.18-7.21 (m, 2H) 6.60-6.70 (m, 2H); ; 3.75 (s, 2H). DSI/NH_3)MS: 157$(M+H)^+$; 174$(M+NH_4)^+$.



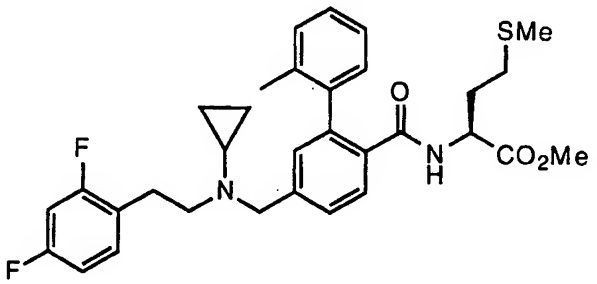
Example 1275C

Prepared according to the procedure of example 1258A from the reaction between example 1275B and cyclopropylamine. NMR(CDCl3) 7.18-7.21 (m, 1H); 6.74-6.82 (m, 2H); 2.80-2.90 (m, 2H); 2.80-2.90 (m, 2H); 1.80-1.98 (m, 1H); 0.40-0.60 (m, 4H); (DSI/NH_3)MS: 198$(M+H)^+$.



Example 1275D

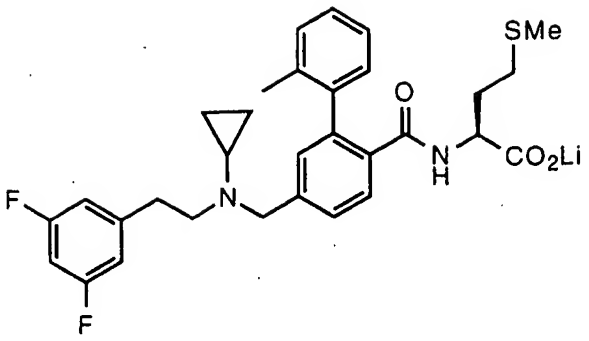
Prepared according to the procedure of example of 1258A from the reaction between example 1275C and 4-formyl-2-(2-methylphenyl)benzoic acid methyl ester. NMR 7.94-8.00 (m, 1H); 7.00-7.40 (m, 7H); 6.74-6.82 (m, 2H); 3.83 (s, 2H); 3.60 (s, 3H); 2.70-2.90 (m, 4H); 2.05 (s, 3H); 1.80-2.00 (m, 1H); 0.40-0.60 (m, 4H); (DSI/NH_3)MS: 436$(M+H)^+$.



Example 1275E

N-[4-*N*-(*N*-cyclopropyl-*N*-(2-(2,4-difluorophenyl)ethyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine, methyl ester.

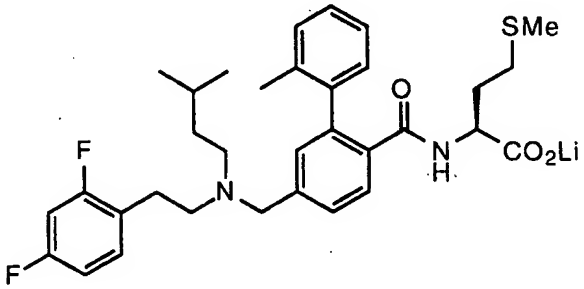
Prepared according to the procedure of example 1258C from 1275D. NMR 7.94-7.80 (m, 1H); 7.00-7.40 (m, 7H); 6.74-6.82 (m, 2H); 5.90-5.94 (m 1H); 4.60-4.70 (m, 1H); 3.83 (s, 2H); 3.75 (s, 3H); 2.80-3.00 (m, 2H); 2.00-2.00 (m, 8H); 1.80-2.00 (m, 2H); 1.50-1.70 (m, 2H); 0.40-0.60 (m, 4H); (DSI/NH_3)MS: 567$(M+H)^+$.



Example 1275F

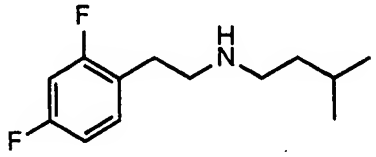
N-[4-*N*-(*N*-cyclopropyl-*N*-(2-(3,5-difluorophenyl)ethyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine lithium salt.

Prepared according to the procedure of example 1178J from 1275E. NMR ^{1}H(MeOH-d4): 7.5-7.6 (1H, m); 7.25-7.35 (1H, m); 7.0-7.25 (7H, m); 6.7-6.8 (2H, m); 4.1-4.25 (1H, m); 3.8 (2H, s); 2.65-2.85 (4H, m); 1.65-2.2 (11H, m); 1.5-1.65 (1H, m); 0.4-0.5 (2H, m); 0.3-0.4 (2H, m). ESI(-)/MS: 551(M-Li). Anal. Calcd for $C_{31}H_{33}N_2O_3SLi \cdot 0.32H_2O \cdot 1.0LiOH$: C, 63.29; H, 5.93; N, 4.76. Found: C, 63.30; H, 5.77; N, 4.67.



Example 1276

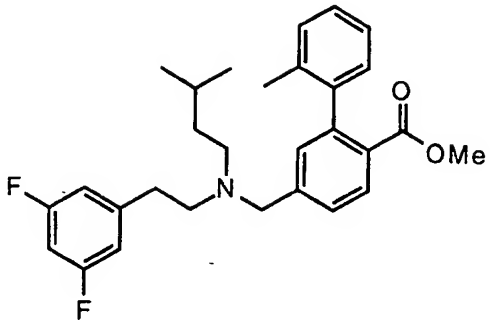
[4-*N*-(*N*-2-methylbutyl-*N*-(2-(2,4-difluorophenyl)ethyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine lithium salt.



Example 1276A

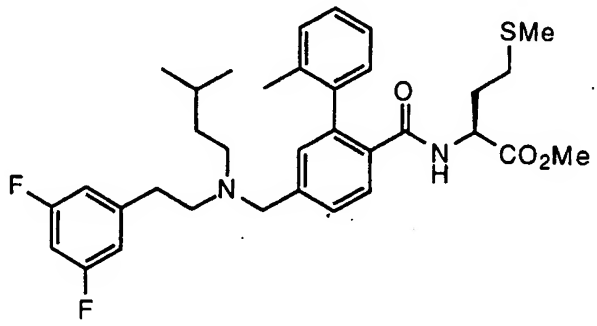
Prepared according to the procedure of example 1275C from example 1275B and 3-methylbutylamine. NMR($CDCl_3$) 7.14-7.22 (m, 1H); 6.74-6.82 (m, 2H); 2.78-2.90 (m,

4H); 2.60-2.68 (m, 2H); 1.50-1.70 (m, 1H); 1.30-1.50 (m, 2H); 0.9 (d, 6H). (DSI/NH_3)MS:.228$(M+H)^+$.



Example 1276B

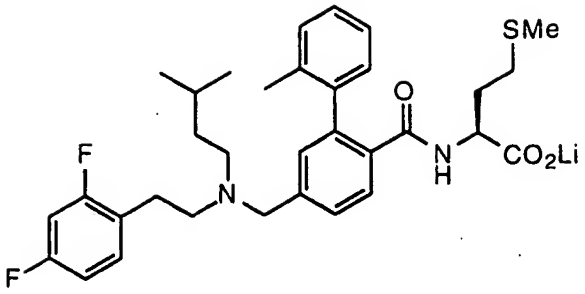
Prepared according to the procedure of example of 1258A from the reaction between example 1276A and 4-formyl-2-(2-methylphenyl)benzoic acid methyl ester. NMR 7.94-8.00 (m, 1H); 7.00-7.40 (m, 7H); 6.74-6.82 (m, 2H); 3.83 (s, 2H); 3.60 (s, 3H); 2.60-2.90 (m, 4H); 2.50-2.60 (m, 2H); 2.05 (s, 3H); 1.40-1.60 (m, 1H); 1.24-1.48 (m, 2H); 0.90 (d, 6H). (DSI/NH_3)MS: 466$(M+H)^+$.



Example 1276C

[4-*N*-(*N*-2-methylbutyl-*N*-(2-(2,4-difluorophenyl)ethyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine, methyl ester.

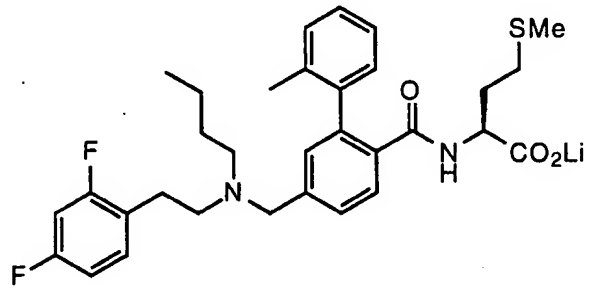
Prepared according to the procedure of example 1258C from 1276B. NMR 7.85-7.95 (m, 1H); 7.00-7.40 (m, 7H); 6.67-6.82 (m, 2H); 5.91-5.97 (m, 1H); 4.56-4.70 (m, 1H); 3.63 (s, 5H); 2.65-2.80 (m, 4H); 2.46-2.55 (m, 2H); 2.00-2.20 (m, 8H); 1.70-2.00 (m, 1H); 1.45-1.70 (m 2H); 1.30-1.40 (m, 2H); 0.90 (d, 6H). (DSI/NH_3)MS: 597$(M+H)^+$.



Example 1276D

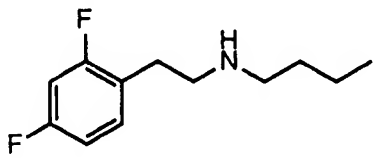
[4-*N*-(*N*-2-methylbutyl-*N*-(2-(2,4-difluorophenyl)ethyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine lithium salt.

Prepared according to the procedure of example 1178J from 1276C. NMR ^{1}H(MeOH-d4): 7.5-7.6 (1H, m); 7.2-7.3 (1H, m); 7.0-7.25 (7H, m); 6.7-6.8 (2H, m); 4.1-4.25 (1H, m); 3.8 (2H, s); 2.65-2.75 (2H, m); 2.55-2.65 (2H, m); 2.4-2.5 (2H, m); 2.1 (1H, s); 1.85-2.0 (6H, m); 1.55-1.85 (2H, m); 1.5-1.65 (1H, m); 1.38-1.5 (1H, m); 1.2-1.38 (2H, m); 0.75)6H, d). ESI(-)/MS: 581(M-Li). Anal. Calcd for $C_{33}H_{39}N_2O_3SLi \cdot 0.25H_2O \cdot 1.8LiOH$: C, 63.30; H, 5.54; N, 4.40. Found: C, 63.30; H, 6.17; N, 4.24.



Example 1277

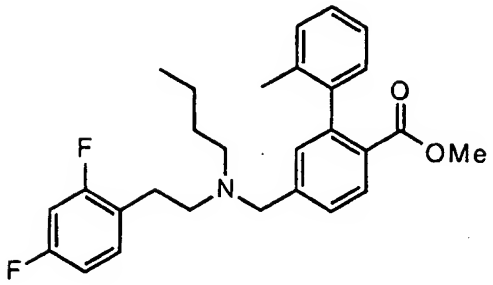
[4-*N*-(*N*-butyl-*N*-(2-(2,4-difluorophenyl)ethyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine lithium salt.



Example 1277A

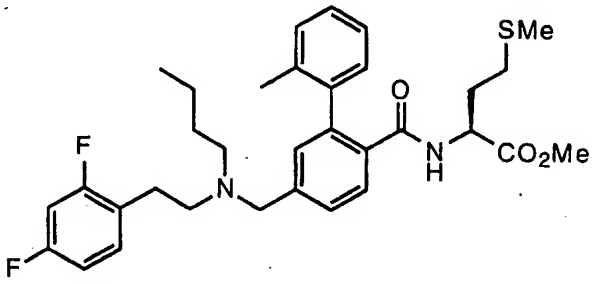
Prepared according to the procedure of example 1275C from example 1275B and butylamine. NMR($CDCl_3$) 7.14-7.22 (m, 1H); 6.74-6.82 (m, 2H); 2.78-2.90 (m, 4H);

2.60-2.68 (m, 2H); 1.50-1.70 (m, 2H); 1.20-1.50 (m, 2H); 0.9 (d, 3H). (DSI/NH_3)MS: 214$(M+H)^+$.



Example 1277B

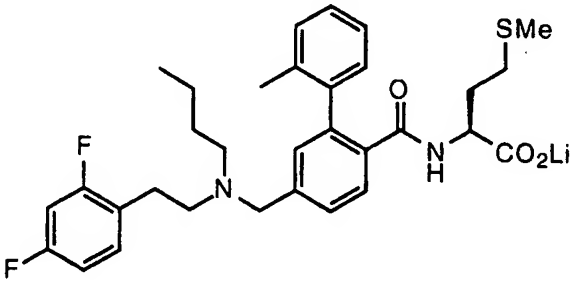
Prepared according to the procedure of example of 1258A from the reaction between example 1277A and 4-formyl-2-(2-methylphenyl)benzoic acid methyl ester. NMR 7.94-8.00 (m, 1H); 7.00-7.40 (m, 7H); 6.74-6.82 (m, 2H); 3.83 (s, 2H); 3.60 (s, 3H); 2.60-2.90 (m, 4H); 2.50-2.60 (m, 2H); 2.05 (s, 3H); 1.40-1.60 (m, 2H); 1.24-1.48 (m, 2H); 0.90 t, 3H). (DSI/NH_3)MS: 452$(M+H)^+$.



Example 1277C

[4-*N*-(*N*-butyl-*N*-(2-(2,4-difluorophenyl)ethyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine, methyl ester.

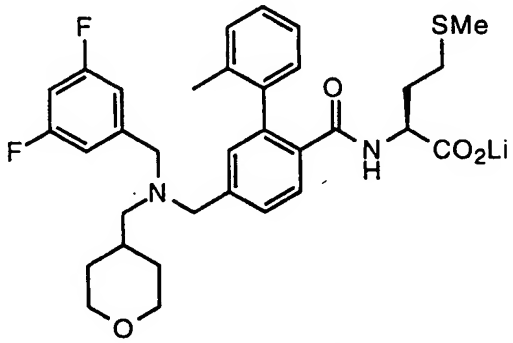
Prepared according to the procedure of example 1258C from 1277B. NMR 7.85-7.95 (m, 1H); 7.00-7.40 (m, 7H); 6.67-6.82 (m, 2H); 5.91-5.97 (m, 1H); 4.56-4.70 (m, 1H); 3.63 (s, 5H); 2.65-2.80 (m, 4H); 2.46-2.55 (m, 2H); 2.00-2.20 (m, 8H); 1.70-2.00 (m, 2H); 1.45-1.70 (m 2H); 1.30-1.40 (m, 2H); 0.90 (t, 3H). (DSI/NH_3)MS: 583$(M+H)^+$.



Example 1277D

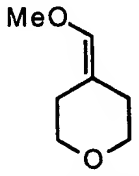
[4-*N*-(*N*-butyl-*N*-(2-(2,4-difluorophenyl)ethyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine lithium salt.

Prepared according to the procedure of example 1178J from 1277C. NMR ^{1}H(MeOH-d4): 7.45-7.55 (1H, m); 7.2-7.5 (1H, m); 7.0-7.25 (7H, m); 6.65-6.75 (2H, m); 4.1-4.25 (1H, m); 3.8 (2H, s); 2.65-2.75 (2H, m); 2.55-2.65 (2H, m); 2.35-2.45 (2H, m); 2.1 (1H, s); 1.8-2.0 (6H, m); 1.65-1.85 (2H, m); 1.4-1.6 (1H, m); 1.25-1.5 (3H, m); 1.1-1.25 (2H, m); 0.75 (3H, t). ESI(-)/MS: 567(M-Li). Anal. Calcd for $C_{33}H_{39}N_2O_3SLi \cdot 1.7H_2O$: C, 63.50; H, 6.73; N, 4.63. Found: C, 63.50; H, 6.41; N, 4.29.



Example 1279

N-[4-*N*-(*N*-(4-methyltetrahydropyran-yl)-*N*-(3,5-difluorobenzyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine lithium salt.

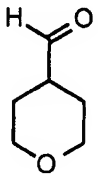


Example 1279A

(Methoxymethyl)triphenylphosphonium chloride (25.71 g, 75 mmol) in 200 ml of anhydrous THF was treated 1.0 M sodium bis(trimethylsilyl)amide solution (75 ml, 75 mmol) at 0°C in 10 min. under N_2. The resulted deep red solution was then stirred at 0°C for another 1 hour. To this solution, tetrahydro-4-*H*-pyran-4-one (5.0 g, 50 mmol) in 10 ml of anhydrous THF was added. After being stirred at 0°C for another 1 hour, the solution was brought up to boiling for 12 hours. The reaction mixture was concentrated under vacuum, then diluted by 1:1ether/hexane solution, filtrated through a pack of silica gel, and washed by another 200 ml of 1:1ether/hexane solution The filtrate was then concentrated. Vacuum distillation of the residue afforded 3.91 g of the title compound (64%).

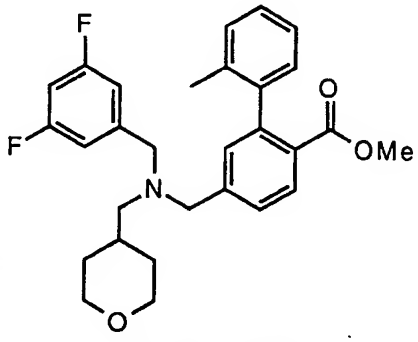
NMR($CDCl_3$) 5.83 (s, 1H); 3.4-3.5 (m, 4H); 3.58 (s, 3H); 2.29-2.35 (m, 2H); 2.05-2.15 (m, 2H). DSI/NH_3)/MS: 129$(M+H)^+$; 146$(M+NH_4)^+$.

16610



Example 1279B

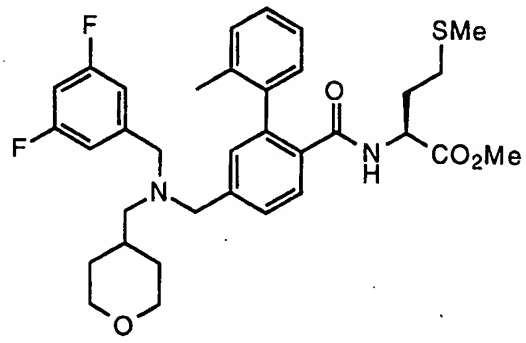
1279A (0.9 g, 7 mmol) in 15 ml of 88% formic acid plus 5 ml of water was refluxed for 3 hours under N_2. After the solvents were removed by rotavapor, the residue 16615 was purified by flash chromatography eluting 3:7 EtOAc/hexane to afford 0.60 g of title compound (75%). NMR($CDCl_3$) 9.62 (s, 1H); 3.85-3.92 (m, 2H); 3.30-3.40 (m, 2H); 1.60-1.85 (m, 3H); 1.05-1.20 (m, 2H). DSI/NH_3)/MS: 115$(M+H)^+$; 132$(M+NH_4)^+$.



16620

Example 1279C

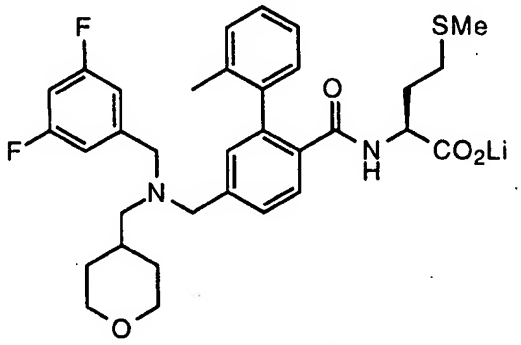
Prepared according to the procedure of example 1258A from reaction between 1258A and 1279B. NMR($CDCl_3$) 7.92-7.99 (m, 1H); 7.35-7.45 (m, 1H); 7.20-7.30 (m, 4H); 7.05-7.10 (m, 1H); 6.82-6.90 (m, 2H); 6.62-6.73 (m, 1H); 3.88-3.98 (m, 2H); 3.61 (s, 3H); 3.59 (s, 2H); 3.52 (s, 2H); 3.25-3.40 (m, 2H); 2.25-2.31 (m, 2H); 2.05 (s, 3H); 16625 1.60-1.90 (m, 3H); 1.00-1.20 (m, 2H). DSI/NH_3)/MS: 480$(M+H)^+$.



Example 1279D

N-[4-*N*-(*N*-(4-methyltetrahydropyran-yl)-*N*-(3,5-difluorobenzyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine lithium salt.

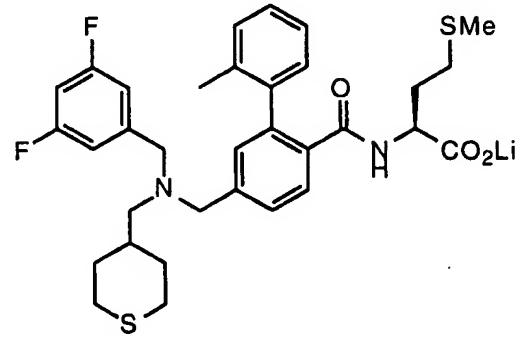
Prepared according to the procedure of example 1258C from 1279C. NMR($CDCl_3$) 7.88-7.99 (m, 1H); 7.35-7.45 (m, 1H); 7.18-7.30 (m, 5H); 6.80-6.90 (m, 2H); 6.62-6.73 (m, 1H); 5.85-5.92 (m, 1H); 4.52-4.70 (m, 1H); 3.88-3.98 (m, 2H); 3.61 (s, 3H); 3.60 (s, 2H); 3.50 (s, 2H); 3.30-3.40 (m, 2H); 2.20-2.31 (m, 2H); 2.0-2.2 (m, 9H); 1.78-1.98 (m, 2H); 1.55-1.78 (m, 3H); 1.00-1.20 (m, 2H). DSI/NH_3)/MS: 611$(M+H)^+$.



Example 1279E

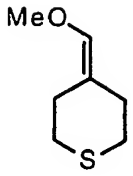
N-[4-*N*-(*N*-(4-methyltetrahydropyran-yl)-*N*-(3,5-difluorobenzyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine lithium salt.

Prepared according to the procedure of example 1178J from 1279D. NMR ^1H(MeOH-d4): 7.6-7.7 (1H, m); 7.38-7.48 (1H, m), 7.0-7.28 (6H, m); 6.9-7.0 (2H, m); 6.78-6.88 (1H, m); 4.1-4.22 (1H, m); 3.8-3.9 (2H, m); 3.8 (2H, s); 3.75 (2H, s); 3.4 (,2H, m); 2.3-2.38 (2H, m); 2.25 (1H, s); 1.76-2.1 (14H, m); 1.0-1.2 (2H, m). ESI(-)/MS: 595(M-Li).Anal. Calcd for $C_{33}H_{37}F_2N_2O_4SLi \cdot 0.52H_2O$: C, 64.76; H, 6.26; N, 4.58. Found: C, 64.76; H, 6.01; N, 4.45.



Example 1280

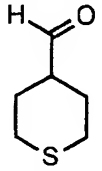
N-[4-*N*-(*N*-(4-methyltetrahydrothiopyran-yl)-*N*-(3,5-difluorobenzyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine lithium salt.



16655

Example 1280A

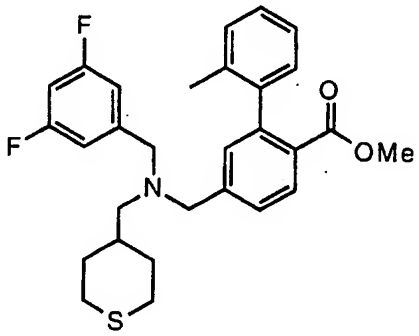
Prepared according to the procedure of example 1279A from tetrahydrothiopyran-4-one. NMR($CDCl_3$) 5.82 (s, 3H); 3.58 (s, 3H); 2.38-2.43 (m, 4H); 2.30-2.38 (m, 2H); 2.05-2.12 (m, 2H). DSI/NH_3)/MS: 145$(M+H)^+$.



16660

Example 1280B

Prepared according to the procedure of example 1279B from 1280A. NMR($CDCl_3$) 9.65 (s, 1H); 2.60-2.80 (m, 4H); 2.20-2.40 (m, 2H); 1.70 1.88 (m, 2H). DSI/NH_3)/MS: 131$(M+H)^+$.

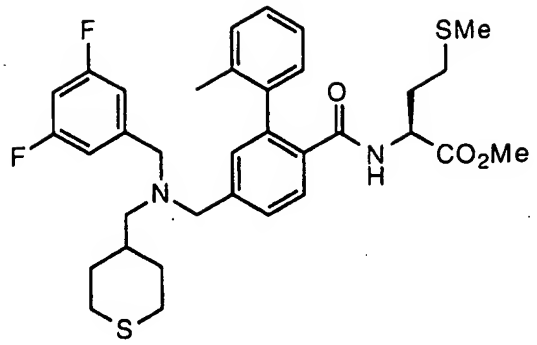


16665

Example 1280C

Prepared according to the procedure of example 1258A from reaction between 1258A and 1280B. NMR($CDCl_3$) 8.00-8.08 (m, 1H); 7.40-7.46 (m, 1H); 7.10-7.30 (m, 4H); 7.05-7.10 (m, 1H); 6.80-6.90 (m, 2H); 6.85-6.73 (m, 1H); 3.60 (S, 5H); 3.50 (s,

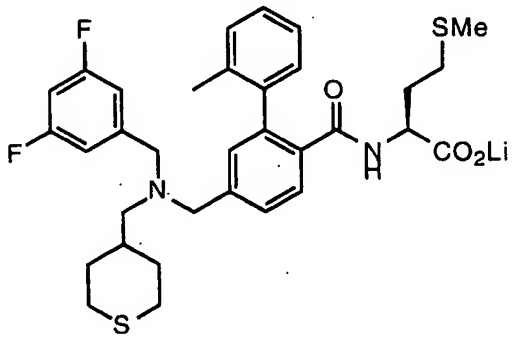
16670 2H); 2.50-2.70 (m, 4H); 2.20-2.30 (m, 2H); 2.00-2.20 (m, 5H); 1.40-1.70 (m, 3H); 1.12-1.30 (m, 2H). DSI/NH_3)/MS: 496$(M+H)^+$.



Example 1280D

16675 *N*-[4-*N*-(*N*-(4-methyltetrahydrothiopyran-yl)-*N*-(3,5-difluorobenzyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine, methyl ester.

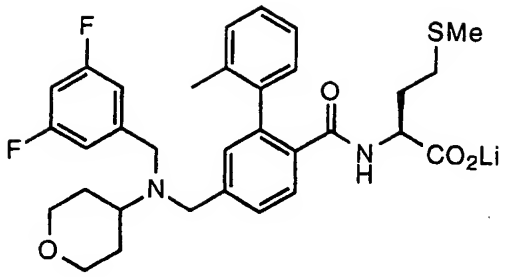
Prepared according to the procedure of example 1258C from 1280C. NMR($CDCl_3$) 7.85-8.00 (m, 1H); 7.1-7.45 (m, 6H); 6.80-6.90 (m, 2H); 6. 65-6.76 (m, 1H); 5.84-5.94 (m, 1H); 4.55-4.70 (m, 1H); 3.65 (s, 3H); 3.52 (s, 2H); 3.45 (s, 2H); 2. 50-2.70 (m, 4H);
16680 2.00-2.30 (m, 13H); 1.78-2.00 (m, 1H); 1.50-1.65 (m, 2H); 1.05-1.30 (m, 2H). DSI/NH_3)/MS: 626$(M+H)^+$.



Example 1280E

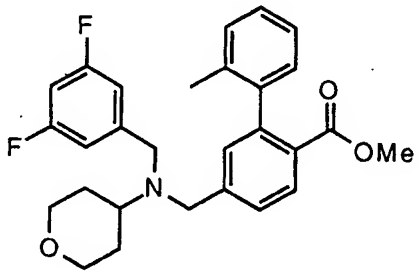
16685 *N*-[4-*N*-(*N*-(4-methyltetrahydrothiopyran-yl)-*N*-(3,5-difluorobenzyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine lithium salt.

Prepared according to the procedure of example 1178J from example 1280D. NMR ^1H(MeOH-d4): 7.6-7.7 (1H, m); 7.38-7.48 (1H, m), 7.0-7.35 (6H, m); 6.9-7.0 (2H, m); 6.75-6.85 (1H, m); 4.1-4.22 (1H, m); 3.6 (2H, s); 3.55(2H, s); 3.35 (2H, s); 2.4-2.65
16690 (4H, m); 2.2-2.3 (3H, m); 1.78-2.1 (8H, m); 1.6-1.78 (2H, m); 1.05-1.2 (2H, m). ESI(-)/MS: 593(M-Li).Anal. Calcd for $C_{33}H_{37}F_2N_2O_4S_2Li \cdot 1.21H_2O \cdot 1.0LiOH$: C, 59.65; H, 6.13; N, 4.22. Found: C, 59.65; H, 5.85; N, 3.89.



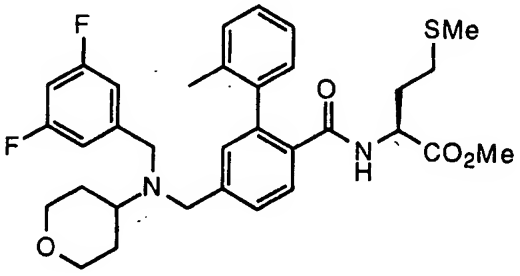
Example 1281

N-[4-*N*-(*N*-(4-tetrahydropyran-yl)-*N*-(3,5-difluorobenzyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine lithium salt.



Example 1281A

Prepared according to the procedure of example 1258A from reaction between 1258A and tetrahydro-4-*H*-pyran-4-one. NMR($CDCl_3$) 7.80-7.95 (m, 1H); 7.35-7.45 (m, 1H); 7.15-7.30 (m, 4H); 7.04-7.10 (m, 1H); 6.80-6.89 (m, 2H); 6.58-6.70 (m, 1H); 3.95-4.03 (m, 2H); 3.70 (s, 2H); 3.65 (s, 2H); 3.60 (s, 3H); 3.20-3.35 (m, 2H); 2.65-2.80 (m, 1H); 2.05 (s, 3H); 1.60-1.80 (m, 4H). (DSI/NH3)/MS: 466$(M+H)^+$.

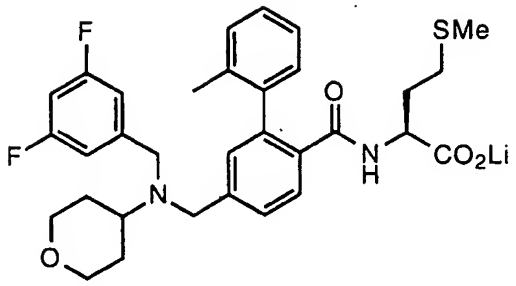


Example 1281B

N-[4-*N*-(*N*-(4-tetrahydropyran-yl)-*N*-(3,5-difluorobenzyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine, methyl ester

Prepared according to the procedure of example 1258C from 1281A. NMR($CDCl_3$) 7.81-7.98 (m, 1H); 7.38-7.45 (m, 1H); 7.20-7.40 (m, 4H); 7.18 (s, 1H); 6.83-6.91 (m, 2H); 6.60-6.70 (m, 1H); 5.81-5.90 (m, 1H); 4.58-4.70 (m, 1H); 3.95-4.02 (m, 2H); 3.70 (s, 2H); 3.63 (s, 2H); 3.60 (s, 2H); 3.20-3.38 (m, 1H); 2.55-2.80 (m, 1H); 1.92-2.20 (m,

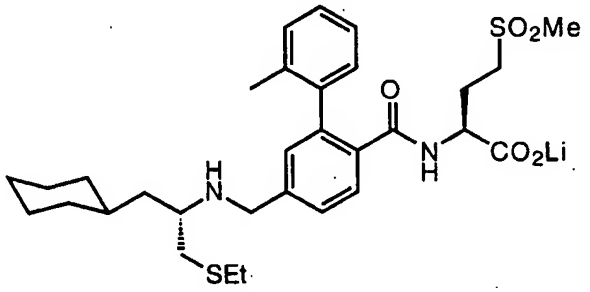
8H); 1.75-1.95 (m, 1H); 1.61-1.78 (m, 3H). 1.50-1.65 (m, 2H); (DSI/NH3)/MS: 597$(M+H)^+$.



Example 1281C

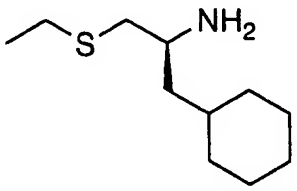
N-[4-*N*-(*N*-(4-tetrahydropyran-yl)-*N*-(3,5-difluorobenzyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine lithium salt.

Prepared according to the procedure of example 1178J from 1281B. NMR ^1H(MeOH-d4): 7.58-7.68 (1H, m); 7.38-7.48 (1H, m), 7.0-7.28 (6H, m); 6.9-7.0 (2H, m); 6.78-6.88 (1H, m); 4.1-4.22 (1H, m); 3.9-4.0 (2H, m); 3.75 (2H, s); 3.7 (2H, s); 3.3 (,2H, m); 2.7-2.85 (1H, m); 2.2 (1H, s); 1.76-2.1 (14H, m). ESI(-)/MS: 586(M-Li). Anal. Calcd for $C_{32}H_{35}F_2N_2O_4SLi \cdot 2.07H_2O$: C, 61.41; H, 6.30; N, 4.37. Found: C, 61.40; H, 6.05; N, 4.37.



Example 1313

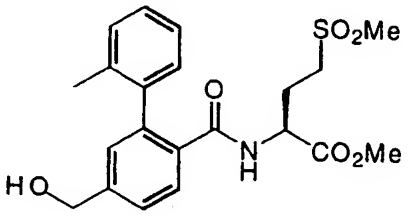
N-[4-(*N*-(3-Cyclohexyl-1-ethylthioprop-2-yl)aminomethyl)-2-(2-methylphenyl)benzoyl]amino-4-methylsulfonylbutanoate Lithium Salt



Example 1313A

2-Amino-3-cyclohexyl-1-ethylthiopropane

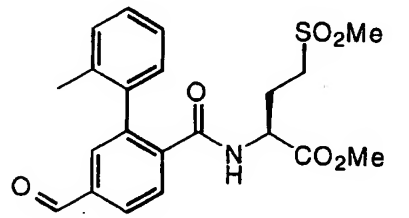
Trifluoroacetic acid (3 mL) was added to a solution of the product from Example 403C (274 mg, 0.9 mmol) in CH_2Cl_2 (3 mL) at ambient temperature. After 30 min of stirring, solvent was removed and the residue redissolved in CH_2Cl_2, washed with a solution of saturated K_2CO_3, dried ($MgSO_4$) and concentrated. The crude product was chromatographed (silica gel; $CHCl_3$/MeOH, 90:10) to afford a clear oil (162 mg, 75%): ^1H NMR ($CDCl_3$, 300 MHz) δ 2.97 (m, 1H), 2.68 (dd, J=13, 4 Hz, 1H), 2.55 (q, J=7.5 Hz, 2H), 2.34 (dd,J=13, 8.5 Hz, 1H), 1.80-1.61 (m, 5H), 1.50-1.10 (m, 6H), 1.26 (t, J=7.5 Hz, 3H), 1.00-0.90 (m, 2H); MS (CI/NH_3) m/z: 202 $(M+H)^+$.



Example 1313B

Methyl-*N*-[4-hydroxymethyl-2-(2-methylphenyl)benzoyl]-2-amino-4-methylsulfonylbutanoate

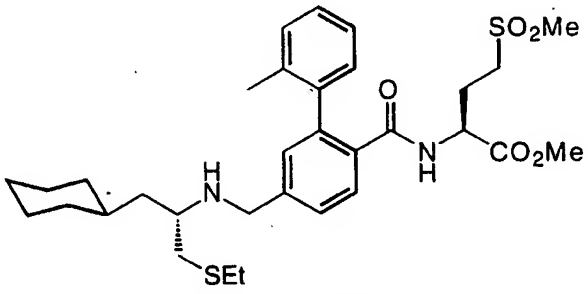
The product from Example 1178C (1.0 g, 4.1 mmol) in MeOH (12 mL) was combined with a solution of saturated LiOH (4.0 mL) and heated at reflux for 3.5 hours. The mixture was allowed to cool to ambient temperature and then extracted with Et_2O. The phases were separated and concentrated HCl added to the aqueous phase which was extracted with EtOAc (2X). The EtOAc phases were combined, dried ($MgSO_4$) and concentrated to dryness to afford the crude acid as a white solid. MS (CI/NH_3) m/z: 243 $(M+H)^+$. The crude acid, EDCI (940 mg, 4.5 mmol), Hobt (1.1 g, 8.2 mmol), (L)-methionine sulfone methyl ester hydrochloride (1.0 mg, 4.5 mmol) and DIEA (2.1 mL, 12.3 mmol) in DMF (15 mL) were allowed to react in a manner similar to that described in Example 608 D. The crude residue was chromatographed (silica gel; MeOH/$CHCl_3$, 5:95) to afford the title compound (963 mg, 56%).



Example 1313C

Methyl-*N*-[4-formyl-2-(2-methylphenyl)benzoyl]-2-amino-4-methylsulfonylbutanoate

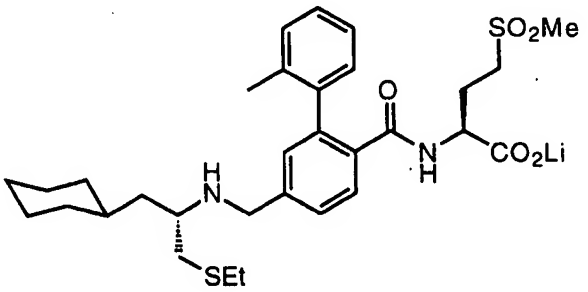
Dimethylsulfoxide (325 µL, 4.6 mmol) was added to a solution of oxalyl chloride (200 µL, 2,5 mmol) at -78 °C. After stirring for 5 min, the product from Example 1313B (955 mg, 2.3 mmol) in CH_2Cl_2 (2.5 mL) was added to the reaction vessel. After 15 min, TEA (950 µL, 6.8 mL) was added to the reaction mixture and the cold bath was removed. After stirring for 30 min, a solution of 2N HCl was added to the mixture and the phases separated. The organic phase was dried ($MgSO_4$) and concentrated. The residue was chromatographed (silica gel; MeOH/$CHCl_3$, 2:98) to afford a clear oil (866 mg, 91%). ^1H NMR ($CDCl_3$, 300 MHz) δ 1.88 (m, 1H), 2.11-2.30 (m, 4H), 2.47-2.73 (m, 2H), 2.71 (s, 3H), 3.71 (s, 3H), 4.65 (m, 1H), 6.12 (dd, J=8 8 Hz, 1H), 7.20 (d, J=7 Hz, 1H), 7.27-7.41 (m, 2H), 7.76 (s, 1H), 7.95-8.06 (m, 2H), 10.10 (s, 1H); MS (CI/NH_3) m/z: 418 $(M+H)^+$.



Example1313D

Methyl-*N*-[4-(*N*-(3-Cyclohexyl-1-ethylthioprop-2-yl)aminomethyl)-2-(2-methylphenyl)benzoyl]amino-4-methylsulfonylbutanoate

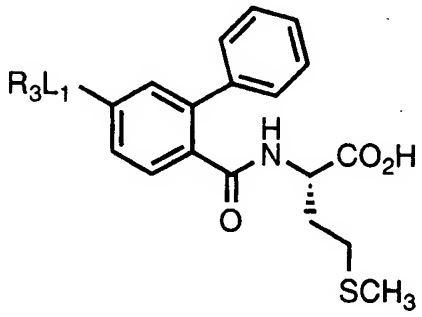
The product from Example 1313A (285 mg, 1.4 mmol), the product from Example 1313C (618 mg, 1.5 mmol) and sodium triacetoxyborohydride (415 mg, 2.0 mmol) were combined in 1,2-dichloroethane (6 mL) at ambient temperature and allowed to stir for 18 hours. A solution of saturated $NaHCO_3$ was added and the mixture was extracted with EtOAc (2X). The EtOAc phases were combined, dried ($MgSO_4$) and concentrated. The residue was chromatographed (silica gel; MeOH/$CHCl_3$, 2:98) to afford a clear oil (753 mg, 89%). MS (CI/NH_3) m/z: 418 $(M+H)^+$.



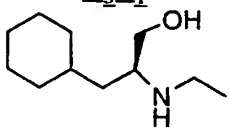
Example 1313E

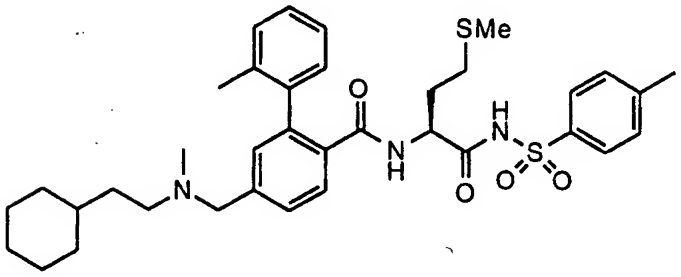
N-[4-(*N*-(3-Cyclohexyl-1-ethylthioprop-2-yl)aminomethyl)-2-(2-methylphenyl)benzoyl]amino-4-methylsulfonylbutanoate Lithium Salt

The product from Example 1313D (748 mg, 1.2 mmol) was allowed to react with lithium hydroxide monohydrate (55 mg, 1.3 mmol) in a manner similar to that described in Example 608E to afford the title compound. ^{1}H NMR (DMSO-d$_6$, 300 MHz) δ 0.70-0.91 (m, 2H), 1.12-1.65 (m, 14H), 1.75-2.20 (m, 5H), 2.35-2.67 (m, 7H), 2.82 (s, 3H), 3.66-3.86 (m, 3H), 6.95 (m, 1H), 7.10-7.25 (m, 4H), 7.38 (d, J=8 Hz,1H), 7.53 (d, J=8 Hz, 1H); MS (APCI(-)) m/z: (M-H)$^-$ 587; Anal. Calcd for $C_{31}H_{43}LiN_2O_5S_2 \cdot 1.90\ H_2O$: C, 59.20; H, 7.50; N, 4.45. Found: C, 59.22; H, 7.16; N, 4.36.



Example 1317

Example	R_3L_1	MS (M+H)±
1317		499

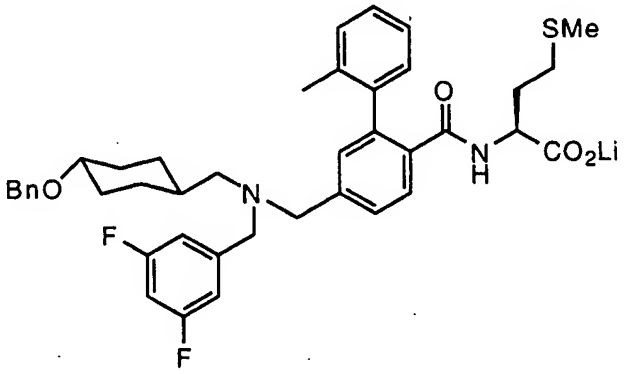


Example 1319

N-[4-(N-Methyl-N-(2-cyclohexylethyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine p-tolylsulfonimide

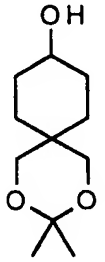
The above compound was prepared from the compound described in Example 608E and p-toluenesulfonamide by the method of Example 1216A, except the reaction was

worked up by diluting with $CHCl_3$ (instead of EtOAc), there was no HCl wash, and the chromatography was done with EtOAc/water/CH_3CO_2H 19/0.5/0.5, then 18/1/1. ^1H NMR ($CDCl_3$) δ 7.80 (m, 3H), 7.58 (dd, 1H), 7.22 (m, 7H), 6.18 (m, 1H), 4.20 (m, 1H), 3.98 (s, 2H), 2.80 (m, 2H), 2.55 (s, 3H), 2.40 (s, 3H), 2.00 (m, 8H), 1.60 (m, 8H), 1.40, 1.20. 0.90 (all m, total 7H). MS (ESI) 648 $(M-H)^-$. Anal calcd for $C_{36}H_{47}N_3O_4S_2 \cdot 1.00$ H_2O: C, 64.74; H, 7.39; N, 6.29. Found: C, 64.53; H, 7.22; N, 6.06.



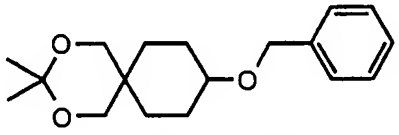
Example 1332

N-[4-*N*-(*N*-(*trans*-4-hydroxycyclohexyl)-*N*-(3,5-difluorobenzyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine lithium salt



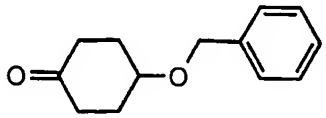
Example 1332A

A mixture of 1,4-cyclohexanedione *mono*-2,2-dimethyltrimethylene ketal (1.98 g, 10 mmol), and sodium borohydride (0.757 g, 20 mmol) in 100 ml of methanol was stirred for 12 hours. The methanol was removed under reduced pressure. The residue was taken into ethyl acetate, washed by 10 % NaOH and brine respectively, and the dried over anhydrous MSG. Yield: 1.60 g (80%). (SDI/NH_3) MS: 201$(M+H)^+$; 218$(M+NH_4)^+$.



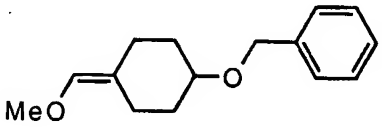
Example 1332B

Prepared according to the procedure of example 1252 from the reaction between example 1332A and benzyl bromide. NMR($CDCl_3$) 7.20-7.35 (m, 5H); 4.57 (s, 2H); 3.45-3.55 (m, 6H); 2.00-2.15 (m, 2H); 1.50-1.82 (m, 5H). (SDI/NH_3) MS: 291$(M+H)^+$; 308$(M+NH_4)^+$.



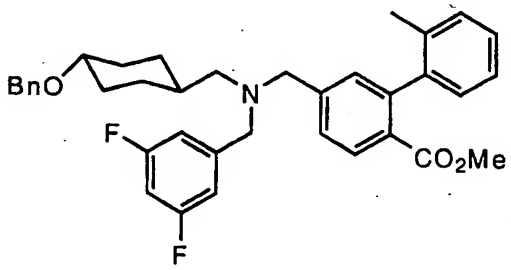
Example 1332C

Prepared according to the procedure of example of example 1266A from the reaction of example 1232B and HCl. NMR($CDCl_3$) 7.23-7.40 (m, 5H); 4.60 (s, 2H); 3.78-4.08 (m, 1H); 2.55-2.70 (m, 2H); 2.20-2.35 (m, 2H); 2.10-2.20 (m, 2H); 1.90-2.01 (m, 2H). (SDI/NH_3) MS: 222$(M+H)^+$; 239$(M+NH_4)^+$.



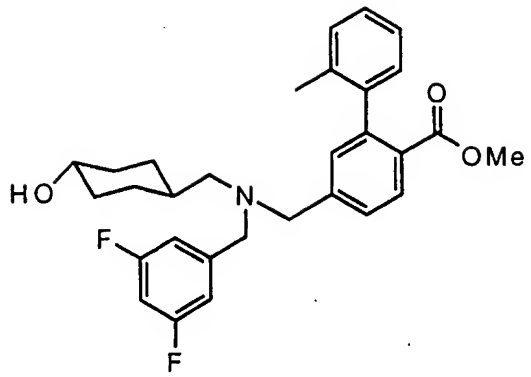
Example 1332D

Prepared according to the procedure of example 1279A from the reaction between example 1232C and (Methoxymethyl)triphenylphosphonium chloride. NMR($CDCl_3$) 7.23-7.40 (m, 5H); 5.85 (s, 1H); 4.60 (s, 2H); 3.63-3.75 (m, 5H); 2.58-2.70 (m, 1H); 2.10-2.30 (m, 1H); 1.4-2.0 (m, 5H). (SDI/NH_3) MS: 233$(M+H)^+$; 250$(M+NH_4)^+$.



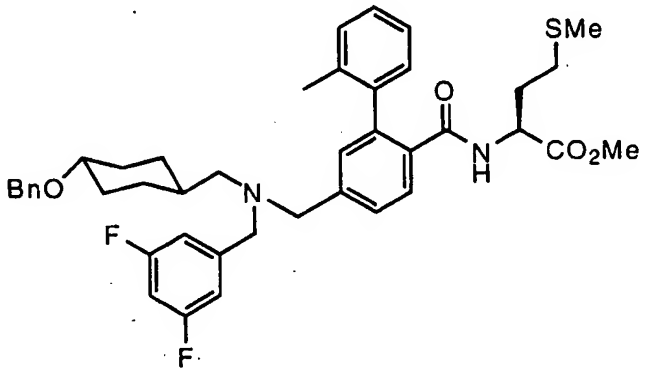
Example 1332E

Example 1332D was hydrolyzed in formic acid according to the example 1279B to give corresponding aldehyde, which was used to react with example 1258A to give two isomers. One is example 1232E, the other is example 1233A. NMR($CDCl_3$) 7.90-7.95 (m, 1H); 7.38-7.44 (m, 1H); 7.13-7.39 (m, 9H); 7.02-7.10 (m, 1H); 6.83-6.92 (m, 2H); 6.60-6.70 (m, 1H); 4.55 (s, 2H); 3.60 (s, 3H); 3.55 (m, 2H); 3.50 (m, 2H); 3.18-4.30 (m, 1H); 2.18-2.21 (m, 2H); 2.0-2.18 (m, 4H); 1.80-2.00 (m, 2H); 1.40-1.60 (m, 2H); 1.09-1.32 (m, 2H); 0.67-0.83 (m, 2H). (SDI/NH_3) MS: 584$(M+H)^+$.



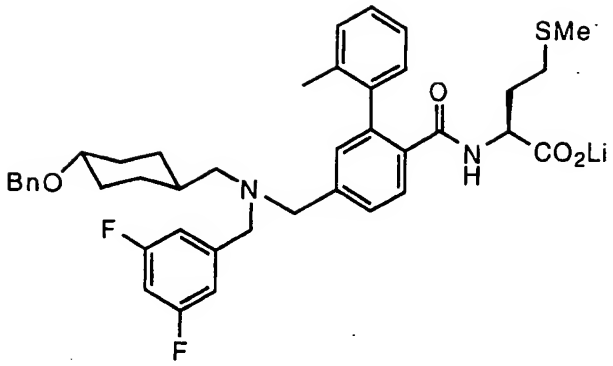
Example 1332F

A mixture of 1332D (0.07 g, 0.12 mmol) and 0.1 ml of trimethylsiliy iodide in 2 ml of methylene chloride was stirred until TLC indicated that there was no starting material left. Flash chromatography of the residue afforded 0.042 g of the title compound (71%). NMR($CDCl_3$) 7.90-7.95 (m, 1H); 7.40-7.44 (m, 1H); 7.13-7.39 (m, 4H); 7.02-7.10 (m, 1H); 6.83-6.92 (m, 2H); 6.60-6.70 (m, 1H); 3.60 (s, 3H); 3.55 (m, 2H); 3.50 (m, 2H); 3.18-4.30 (m, 1H); 2.18-2.21 (m, 2H); 2.0-2.18 (m, 4H); 1.80-2.00 (m, 2H); 1.40-1.60 (m, 2H); 1.09-1.32 (m, 2H); 0.67-0.83 (m, 2H). (SDI/NH_3) MS: 494$(M+H)^+$.



Example 1332G

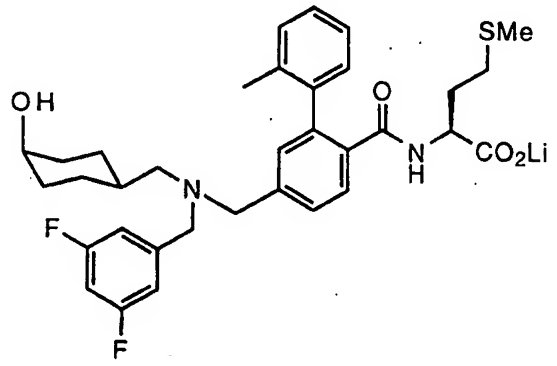
Prepared according to the procedure of example 1258C from example 1232F. NMR($CDCl_3$) 7.83-7.95 (m, 1H); 7.40-7.44 (m, 1H); 7.13-7.40 (m, 4H); 7.02-7.10 (m, 1H); 6.83-6.92 (m, 2H); 6.60-6.70 (m, 1H); 5.84-5.90 (m, 1H); 4.55-4.67 (m, 1H); 3.60 (s, 3H); 3.55 (m, 2H); 3.50 (m, 2H); 3.18-4.30 (m, 1H); 2.18-2.21 (m, 2H); 1.80-2.25 (m, 16H); 1.40-1.60 (m, 2H); 1.09-1.32 (m, 2H); 0.67-0.83 (m, 2H). (SDI/NH_3) MS: 624$(M+H)^+$.



Example 1332H

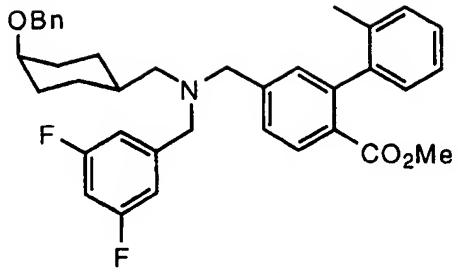
N-[4-*N*-(*N*-(*trans*-4-hydroxycyclohexyl)-*N*-(3,5-difluorobenzyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine lithium salt

Prepared according to the procedure of example 1178J from example 1332G. NMR($CDCl_3$) 7.60-7.70 (m, 1H); 7.40-7.44 (m, 1H); 7.13-7.40 (m, 5H); 6.83-7.00 (m, 2H); 6.68-6.72 (m, 1H); 4.20-4.30 (m, 1H); 3.60 (m, 2H); 3.55 (m, 2H); 3.18-4.30 (m, 1H); 2.18-2.21 (m, 2H); 1.80-2.25 (m, 16H); 1.40-1.60 (m, 2H); 1.09-1.32 (m, 2H); 0.67-0.83 (m, 2H). ESI(-)/MS: 609(M-Li). Anal. Calcd for $C_{34}H_{39}F_2N_2O_4SLi \cdot 2.00$ LiOH: C, 61.45; H, 6.22; N, 4.22. Found: C, 61.56; H, 5.88; N,3.94.



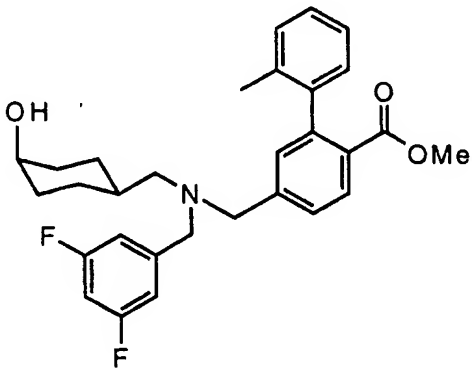
Example 1333

N-[4-*N*-(*N*-(*cis*-4-hydroxycyclohexyl)-*N*-(3,5-difluorobenzyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine lithium salt



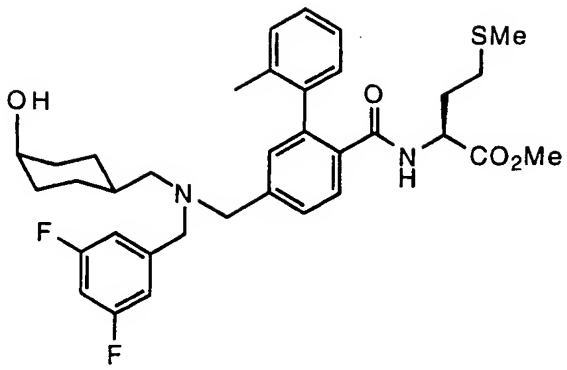
Example 1333A

Prepared according to the procedure of example 1332E. NMR($CDCl_3$) 7.90-7.95 (m, 1H); 7.38-7.44 (m, 1H); 7.13-7.39 (m, 9H); 7.02-7.10 (m, 1H); 6.83-6.92 (m, 2H); 6.60-6.70 (m, 1H); 4.55 (s, 2H); 3.90-4.00 (m, 1H); 3.60 (s, 3H); 3.55 (m, 2H); 3.50 (m, 2H); 3.18-4.30 (m, 1H); 2.18-2.21 (m, 2H); 2.0-2.18 (m, 3H); 1.80-2.00 (m, 2H); 1.40-1.60 (m, 2H); 1.09-1.32 (m, 2H); 0.67-0.83 (m, 2H). (SDI/NH_3) MS: 584$(M+H)^+$.



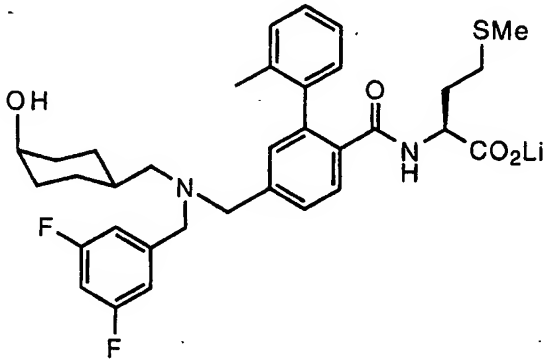
Example 1333B

Prepared according to the procedure of example 1332F from the reaction between 1333B and trimethylsilyl iodide. NMR($CDCl_3$) 7.90-7.95 (m, 1H); 7.40-7.44 (m, 1H); 7.13-7.39 (m, 4H); 7.02-7.10 (m, 1H); 6.83-6.92 (m, 2H); 6.60-6.70 (m, 1H); 3.90-4.00 (m, 1H); 3.60 (s, 3H); 3.55 (m, 2H); 3.50 (m, 2H); 3.18-4.30 (m, 1H); 2.18-2.21 (m, 2H); 2.0-2.18 (m, 3H); 1.80-2.00 (m, 2H); 1.40-1.60 (m, 2H); 1.09-1.32 (m, 2H); 0.67-0.83 (m, 2H). (SDI/NH_3) MS: 494$(M+H)^+$.



Example 1333C

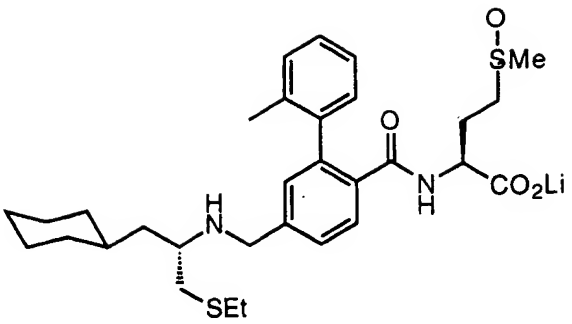
Prepared according to the procedure of example 1258C from example 1333B. NMR($CDCl_3$) 7.83-7.95 (m, 1H); 7.40-7.44 (m, 1H); 7.13-7.40 (m, 4H); 7.02-7.10 (m, 1H); 6.83-6.92 (m, 2H); 6.60-6.70 (m, 1H); 5.84-5.90 (m, 1H); 4.55-4.67 (m, 1H); 3.92-4.02 (m, 1H); 3.60 (s, 3H); 3.55 (m, 2H); 3.50 (m, 2H); 3.18-4.30 (m, 1H); 2.18-2.21 (m, 2H); 1.80-2.25 (m, 15H); 1.40-1.60 (m, 2H); 1.09-1.32 (m, 2H); 0.67-0.83 (m, 2H). (SDI/NH_3) MS: 624$(M+H)^+$.



Example 1333D

N-[4-*N*-(*N*-(*cis*-4-hydroxycyclohexyl)-*N*-(3,5-difluorobenzyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine lithium salt

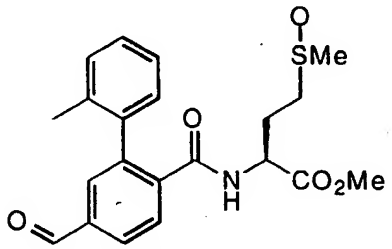
Prepared according to the procedure of example 1178J from example 1333C. NMR($CDCl_3$) 7.60-7.70 (m, 1H); 7.40-7.44 (m, 1H); 7.13-7.40 (m, 5H); 6.83-7.00 (m, 2H); 6.68-6.72 (m, 1H); 4.20-4.30 (m, 1H); 3.92-4.01 (m, 1H); 3.60 (m, 2H); 3.55 (m, 2H); 3.18-4.30 (m, 1H); 2.18-2.21 (m, 2H); 1.80-2.25 (m, 15H); 1.40-1.60 (m, 2H); 1.09-1.32 (m, 2H); 0.67-0.83 (m, 2H). ESI(-)/MS: 609(M-Li). Anal. Calcd for $C_{34}H_{39}F_2N_2O_4SLi \cdot 2.50\ LiOH \cdot 0.57H_2O$: C, 62.58; H, 6.26; N, 4.29. Found: C, 61.61; H, 5.99 N,3.92.



Example 1334

(2S) 2-N-[4-(1-ethylthio-3-cyclohexylprop-2-ylaminomethyl)-2-(2-methylphenyl)benzoyl]amino-4-methylsulfenylbutanoate Lithium Salt

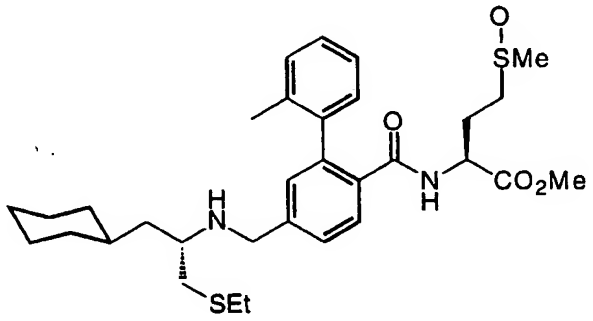
16945



Example 1334A

(2S) 2-N-[4-formyl-2-(2-methylphenyl)benzoyl]amino-4-methylsulfenylbutanoate, Methyl Ester

16950 The title compound was prepared from N-[4-formyl-2-(2-methylphenyl)benzoyl]methionine methyl ester (example 403G) according to the procedure in example 1071D, and was isolated as a light yellow oil. MS(APCI(+)) 402 $(M+H)^+$. MS(APCI(-)) 436 $(M+Cl)^-$, 400 $(M-H)^-$.



16955

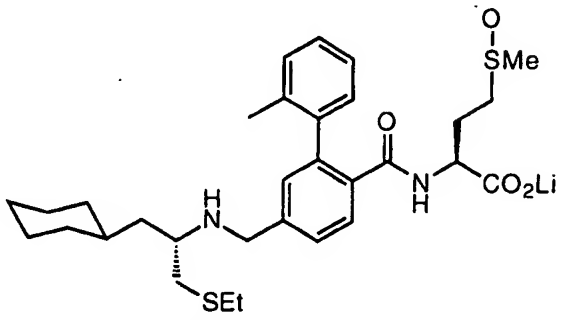
Example 1334B

(2S) 2-N-[4-(1-ethylthio-3-cyclohexylprop-2-ylaminomethyl)-2-(2-methylphenyl)benzoyl]amino-4-methylsulfenylbutanoate, Methyl Ester

The title compound was prepared according to example 403H, substituting (2S) 2-N-

16960 [4-formyl-2-(2-methylphenyl)benzoyl]amino-4-methylsulfenylbutanoate methyl ester for N-

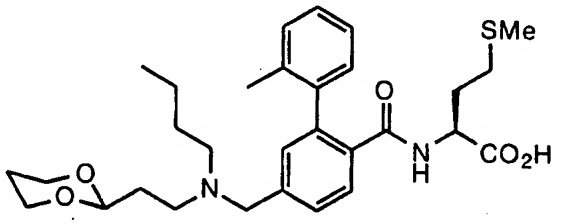
[4-formyl-2-(2-methylphenyl)benzoyl]methionine methyl ester. MS(APCI(+)) 587 $(M+H)^+$. MS(APCI(-)) 621 $(M+Cl)^-$.



Example 1334C

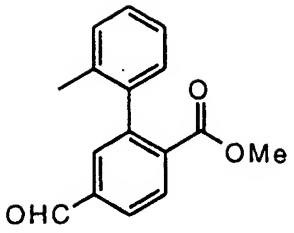
(2S) 2-N-[4-(1-ethylthio-3-cyclohexylprop-2-ylaminomethyl)-2-(2-methylphenyl)benzoyl]amino-4-methylsulfenylbutanoate, Lithium Salt

The title compound was prepared from (2S) 2-N-[4-(1-ethylthio-3-cyclohexylprop-2-ylaminomethyl)-2-(2-methylphenyl)benzoyl]amino-4-methylsulfenylbutanoate methyl ester according to the procedure in example 608E, with the exception that the product was isolated as a light yellow foam after concentrating a methanolic solution under reduced pressure. ^1H NMR (300 MHz, DMSO) δ 0.66-0.90 (m, 2H), 1.02-1.80 (m, 13H), 1.10 (t, J=7.2 Hz, 3H), 1.96-2.21 (m, 5H), 2.36 (s, 1.5H), 2.39 (s, 1.5H), 2.41 (q, J=7.2 Hz, 2H), 2.56-2.67 (m, 3H), 3.60-3.84 (m, 4H), 6.98 (brd, J=6 Hz, 1H), 7.08-7.23 (m, 5H), 7.38 (d, J=8.4 Hz, 1H), 7.49 (d, J=7.8 Hz, 0.5H), 7.51 (d, J=7.8 Hz, 0.5H). MS (APCI(-)) m/e 571 (M-H).



Example 1335

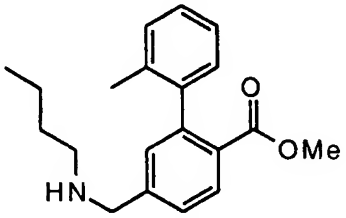
N-[4-(*N*-(2-(1,3-dioxan-2-ylethyl)-*N*-butylaminomethyl)-2-(2-methylphenyl)benzoyl]methionine



Example1335A

4-Formyl-2-(2-methylphenyl)benzoic acid methyl ester

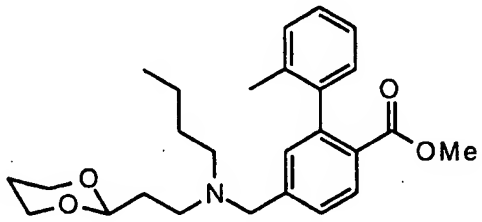
Following the procedure of example 1134D, example 1178 C (3.30 g, 11.82 mmol) provided 3.00 g 100%) of the title compound. MS (DCI, NH_3): 255 (MH^+).



Example 1335B

4-n-Butylaminomethyl-2-(2-methylphenyl)benzoic acid methyl ester

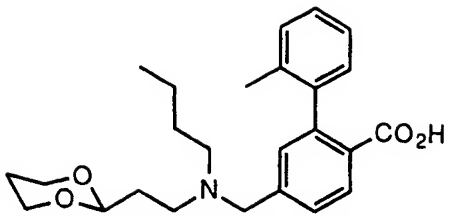
Following the procedure of example 1106D, part 1 example 1335A (1.27 g, 5.00 mmol) and butyl amine (0.99 mL, 10.00 mmol) provided 1.45 g (94%) of the title compound. MS (DCI, NH_3): 312 (MH^+).



Example 1335C

4-(*N*-(2-(1,3-dioxan-2-ylethyl)-*N*-butylaminomethyl)-2-(2-methylphenyl)benzoic acid, methyl ester

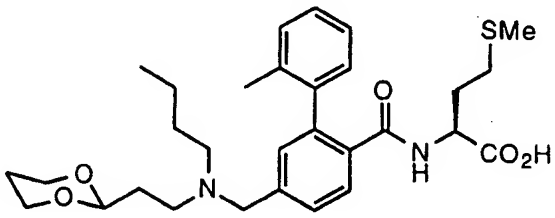
A solution of example 1335B (359 mg 1.15 mmol), 2-bromoethyl-1,3-dioxane (164 µL, 1.2 mmol), TBAI (443 mg, 1.2 mmol) and diiospropylethylamine (260 µL, 1.5 mmol) in 3 mL of DMF were heated to 60°C for 72 hours. The cooled reaction mixture was diluted with water and extracted with 3 portions of ethyl ether. The combined organic extracts were washed with water, brine, dried, filtered and concentrated. The residue was purified by column chromatography on silica gel (25 g, 25% ethyl acetate/hexanes) provided 330 mg (78%) of the title compound. MS: (ESI+) 426 (MH^+).



Example 1335D

4-(*N*-(2-(1,3-dioxan-2-ylethyl)-*N*-butylaminomethyl)-2-(2-methylphenyl)benzoic acid,

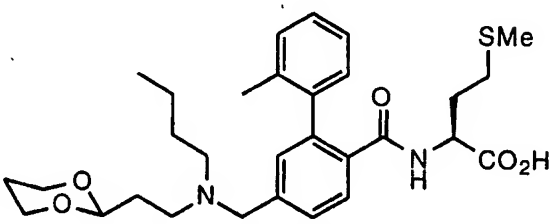
Following the procedure of example 1130D, example1335C (310 mg, 0.72 mmol) provided 222 mg (75%) of the title compound. MS (ESI+): 412 (MH+): (ESI-): 410 (M-H).



Example 1335E

N-[4-(*N*-(2-(1,3-dioxan-2-ylethyl)-*N*-butylaminomethyl)-2-(2-methylphenyl)benzoyl]methionine, methyl ester

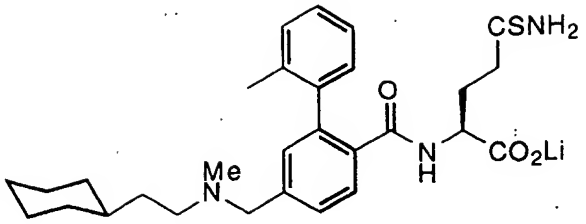
Following the procedure of example 1178I, example1335D (85 mg, 0.25 mmol) provided 57 mg (50%) of the title compound. MS (ESI+): 557 (MH+): (ESI-): 555 (M-H).



Example 1335F

N-[4-(*N*-(2-(1,3-dioxan-2-ylethyl)-*N*-butylaminomethyl)-2-(2-methylphenyl)benzoyl]methionine

Following the procedure of example 1104D, example1335 E (55 mg (0.10 mmol) provided 30 mg of the title compound. ^{1}H nmr (300 MHz., CD_3OD): δ 7.64, d, 1H; 7.49, dd, 1H; 7.29, m, 1H; 7.02 - 7.22, m, 4H; 4.64, t, 1H; 4.29, m, 3H; 3.91, ddd, 2H; 3.66, dt, 2H; 3.22, m, 2H; 3.03, m, 2H; envelope 1.74 - 2.16, m, 12H; 1.62, m, 3H; 1.18 - 1.36, mn, 3H; 0.88, t, 3H. MS (ESI+): 543 (MH+): (ESI-): 541 (M-H). Calc'd for $C_{31}H_{43}N_2O_5S \cdot 1.30\ H_2O$; C 63.64; H 7.94; N 4.95; Found: C 63.63; H 7.37; N 5.07.



Example 1336

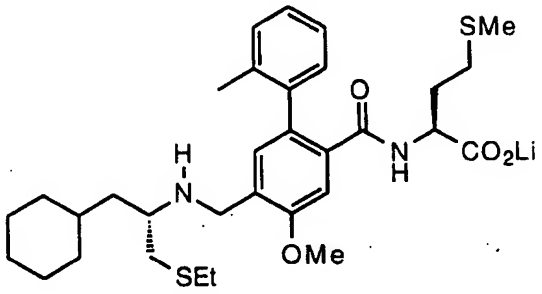
N-[4-(*N*-(2-cyclohexylethyl)-*N*-methylaminomethyl)-2-(2-methylphenyl)benzoyl]thioglutamine Lithium Salt

N-[4-(*N*-(2-cyclohexylethyl)-*N*-methylaminomethyl)-2-(2-methylphenyl)benzoyl]thioglutamine methyl ester (12 mg, 22.9 µmol) was saponified using the standard LiOH procedure, evaporated, and lyophilized from water to provide 9.8 mg of the title compound. MS m/e 514 $(M-H)^-$.

Example 1336B

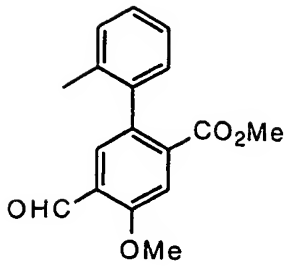
N-[4-(*N*-(2-cyclohexylethyl)-*N*-methylaminomethyl)-2-(2-methylphenyl)benzoyl]thioglutamine Methyl Ester

N-[4-(*N*-(2-cyclohexylethyl)-*N*-methylaminomethyl)-2-(2-methylphenyl)benzoyl]glutaminitrile methyl ester, see Example 1041, (139 mg, 0.28 mmol) was dissolved in 5 mL pyridine with TEA (0.5 mL). Excess H_2S was bubbled into the solution which was then sealed and stirred at room temperature for 18 hours. The reaction was evaporated to dryness, dissolved in EtOAc, washed with water and brine, and chromatographed (50 % EtOAc/hexanes) to give 13 mg of the methyl ester. MS m/e 524 $(M+H)^+$. ^1H NMR ($CDCl_3$, 300 MHz) δ 0.82 (m, 2H), 1.11 (m, 3H), 1.32 (m, 5H), 1.6 (m, 7H), 2.18 (m, 6H), 2.32 (m, 1H), 2.58 (m, 1H), 2.75 (m, 1H), 3.53 (m, 2H), 3.72 (s, 3H), 6.9-7.5 (m, 9H), 7.83 (m, 1H).



Example 1337

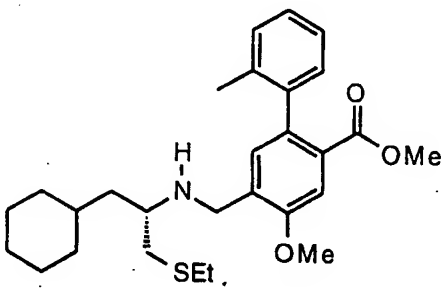
N-[4-(1-ethylthio-3-cyclohexylprop-2-ylaminomethyl)-5-methoxy-2-(2-methylphenyl)benzoyl]methionine



Example 1337A

2-(2-Methylphenyl)-4-formyl-5-methoxybenzoic acid, methyl ester

A solution of example 1134D (180 mg, 0.63 mmol) in 2 mL of DMF was treated with sodium methoxide (102 mg, 1.89 mmol) and the mixture stirred for 3 hours. The solution was diluted with water and extracted with 3 portions of ethyl acetate. The combined organic extracts were wased with water, brine, dried filtered and concentrated. The residue was purified by column chromatography to provide 40g (22%) of the title compound. MS (DCI, NH_3): 302 (M+ NH_4^+).



Example 1337B

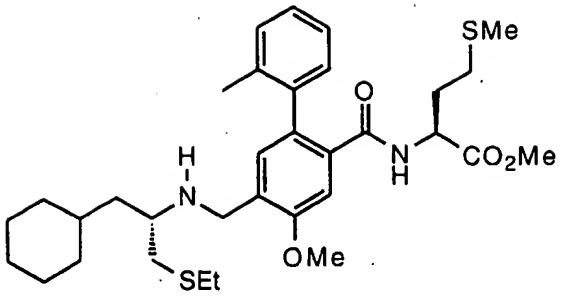
4-(1-ethylthio-3-cyclohexylprop-2-ylaminomethyl)-5-methoxy-2-(2-methylphenyl)benzoic acid, methyl ester

Using the procedure of example 1134E, example 1337A provided the title compound. MS (ESI +): 470 (MH^+); (ESI-) 468 (M-H).

Example 1337C

4-(1-ethylthio-3-cyclohexylprop-2-ylaminomethyl)-5-methoxy-2-(2-methylphenyl)benzoic acid

Using the procedure of example 1134F, example 1337B provided the title compound. MS (ESI +): 456 (MH^+); (ESI-) 454 (M-H).

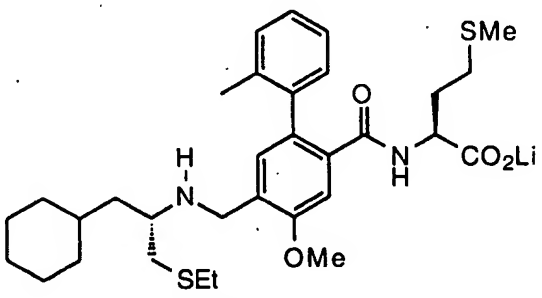


Example 1337D

17085 *N*-[4-(1-ethylthio-3-cyclohexylprop-2-ylaminomethyl)-5-methoxy-2-(2-methylphenyl)benzoyl]methionine, methyl ester

According to the procedure described in example 1178I, example 1137C (55 mg, 0.12 mmol) provided 39 mg (54%) of the title compound. MS (ESI +): 601 (MH^+); (ESI-) 599 (M-H).

17090

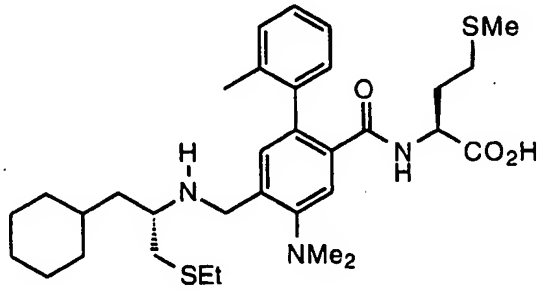


Example 1337

N-[4-(1-ethylthio-3-cyclohexylprop-2-ylaminomethyl)-5-methoxy-2-(2-methylphenyl)benzoyl]methionine

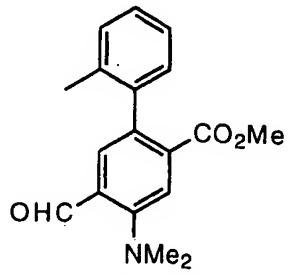
17095 Following the procedure of example 1105D, example 1137D (39 mg, 0.065 mmol) provided the title compound. ^1H NMR (300 MHz, DMSO): δ 7.9 (1H), 7.0-7.3 (5H), 4.1 (1H), 3.9 (1H), 3.3 (3H), 2.7 (1H), 2.4 (3H), 2.0-2.3 (6H), 1.95 (3H), 0.8- 1.9 (22H). Mass spec (ESI): 587 (M+H), 585 (M-H)

17100



Example 1338

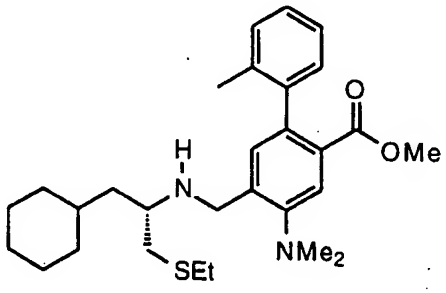
N-[4-(1-ethylthio-3-cyclohexylprop-2-ylaminomethyl)-5-N'N'-dimethylamino-2-(2-methylphenyl)benzoyl]methionine



Example 1338A

2-(2-Methylphenyl)-4-formyl-5-N,N-dimethylaminobenzoic acid, methyl ester

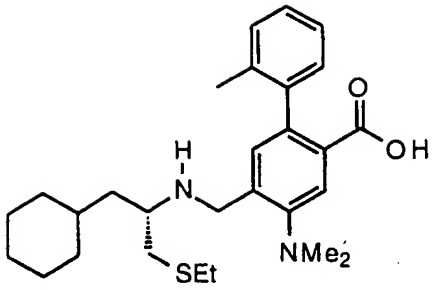
A solution of example 1134D (146 mg, 0.50 mmol) in 1 mL of DMF was treated with 2 mL of 40% aqueous dimethylamine and the mixture heated at 70°C for 2days. The cooled reaction mixture was diluted with water and the pH of the mixture adjusted to 5. The solution was extracted with 3 portions of ethyl acetate adnt he combined organic extracts were washed with wate and brine, dried, filtered and concentrated. The residue was dissolved in ethyl acetate and treated with ethereal diazomethane until tlc analysis indicated no more acid present. This solution was concentrated and the residue purified by column chromatography on silica gel (25 g, 15% ethyl acetate/hexanes) to provide 124 mg (87%) of the title compound. MS (DCI, NH_3): 298 (MH^+).



Example 1338B

4-(1-ethylthio-3-cyclohexylprop-2-ylaminomethyl)-5-N',N'-dimethylamino-2-(2-methylphenyl)benzoic acid, methyl ester

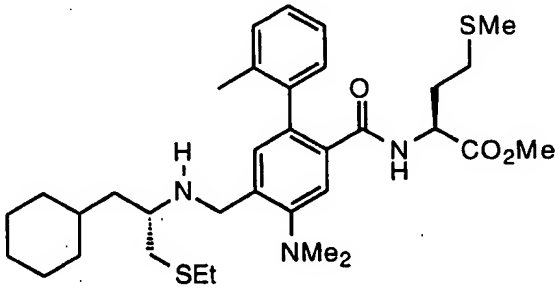
Using the procedure of example 1134E, example 1338A provided the title compound. MS (ESI +): 483 (MH^+); (ESI-) 481 (M-H).



Example 1338C

4-(1-ethylthio-3-cyclohexylprop-2-ylaminomethyl)-5-N',N'-dimethylamino-2-(2-methylphenyl)benzoic acid

17130 Following the procedure of example 1134F, example 1138B provided the title compound. MS (ESI +): 469 (MH^+); (ESI-) 467 (M-H).

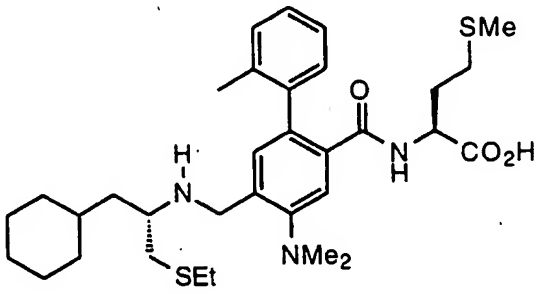


Example 1338D

17135 *N*-[4-(1-ethylthio-3-cyclohexylprop-2-ylaminomethyl)-5-N'N'-dimethylamino-2-(2-methylphenyl)benzoyl]methionine, methyl ester

According to the procedure described in example 1178I, example 1138C (93 mg, 0.20 mmol) provided 69 mg (56%) of the title compound. MS (ESI +): 614 (MH^+); (ESI-) 612 (M-H).

17140



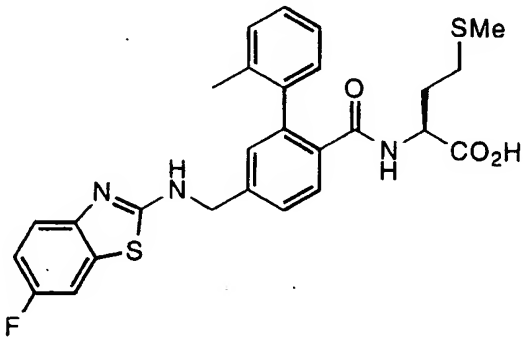
Example 1338E

N-[4-(1-ethylthio-3-cyclohexylprop-2-ylaminomethyl)-5-N'N'-dimethylamino-2-(2-methylphenyl)benzoyl]methionine

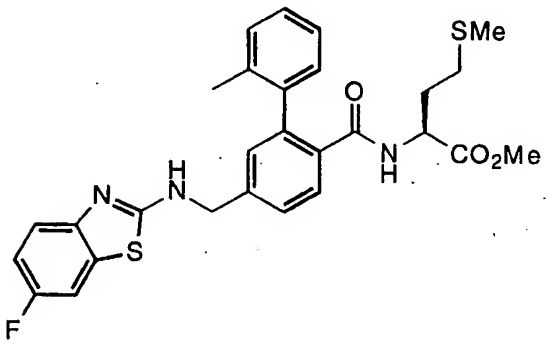
Following the procedure of example 1105D, example 1138D (69 mg, 0.11 mmol) provided the title compound. ^{1}H NMR (300 MHz., DMSO): δ 7.9 (1H), 7.0-7.3 (5H), 4.2 (1H), 3.9 (1H), 2.72 (6H), 2.45 (3H), 2.0-2.2 (6H), 1.9 (3H),0.7-1.85 (22H). Mass spec (ESI): 600 (M+H), 598 (M-H).

Example 1339

Pittsburg example, waiting for experimental data and other information.



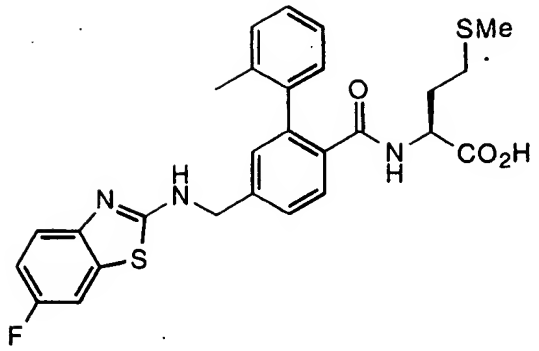
Example1340



Example 1340A

N-[4-*N*-(6-Fluorobenzothiazol-2-yl)aminomethyl-2-(2-methylphenyl)benzoyl]methionine methyl ester

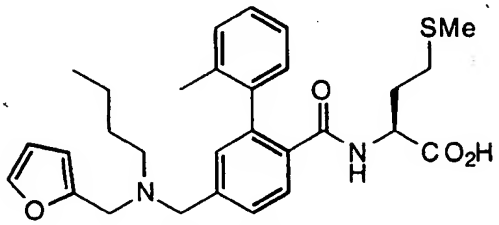
The desired compound was prepared according to the method of Example 1203A starting with *N*-[4-formyl-2-(2-methylphenyl)benzoyl]methionine methyl ester, prepared as in Example 403G, and 2-amino-6-fluorobenzothiazole. m/e (ESI) 538 (MH^+)



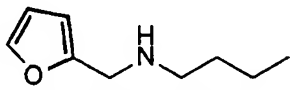
Example 1340B

N-[4-*N*-(6-Fluorobenzothiazol-2-yl)aminomethyl-2-(2-methylphenyl)benzoyl]methionine

The desired compound was prepared according to the method of Example 403I starting with the compound in Example 1340A. ^{1}H (300MHz, $CDCl_3$, δ) 7.91 (1H, m), 7.51 (1H, m), 7.34 (2H, m), 7.30-7.15 (4H, m), 7.05 (3H, m), 5.99 (1H, m), 4.59 (1H, m), 4.48 (2H, bd, J=8Hz), 2.20-1.80 (9H, m), 1.72 (1H, m). m/e (ESI) 522 (MH^-) Anal.calc. for $C_{27}H_{26}FN_3O_3S_2 \cdot 0.25\ H_2O$ C 61.40, H 5.06, N 7.96 Found C 61.38, H 4.56, N 7.73



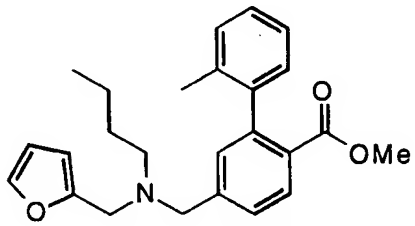
Example 1341



Example 1341A

N--Butyl-*N*-(furan-2-ylmethyl)amine

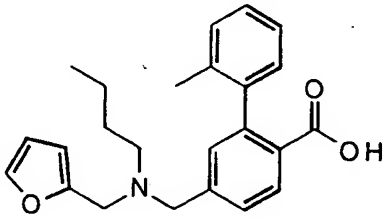
The desired amine was prepared using the method described in Example 1171A starting with 2-furoic acid and butylamine. m/e (DCI/NH_3) 154 (MH^+)



Example 1341B

4-(*N*-Butyl-*N*-(furan-2-ylmethyl)aminomethyl)-2-(2-methylphenyl)benzoic acid methyl ester

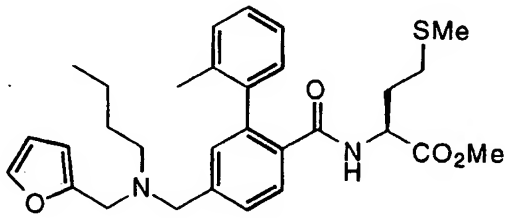
The desired compound was prepared using the method described in Example 1178G starting with *N*--Butyl-*N*-(furan-2-ylmethyl)amine, prepared as in Example 1341A, and 4-bromomethyl-2-(2-methylphenyl)benzoic acid methyl ester, prepared as in Example 1178A-D. m/e (ESI) 392 (MH^+)



Example 1341C

4-(*N*-Butyl-*N*-(furan-2-ylmethyl)aminomethyl)-2-(2-methylphenyl)benzoic acid

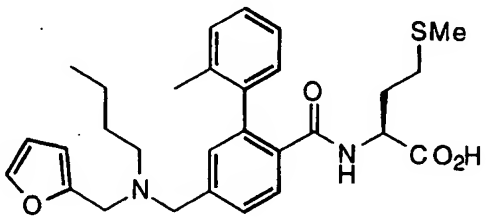
The desired acid was prepared using the method described in Example 403E starting with the compound prepared in Example 1341B.



Example 1341D

N-[4-*N*-Butyl-*N*-(furan-2-ylmethyl)aminomethyl-2-(2-methylphenyl)benzoyl]methionine methyl ester

The desired product was prepared using the method described in Example 403F starting with the compound prepared in Example 1341C. m/e (ESI) 523 (MH^+)



Example 1341E

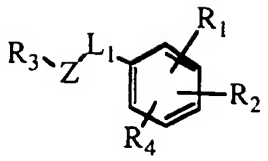
N-[4-*N*-Butyl-*N*-(furan-2-ylmethyl)aminomethyl-2-(2-methylphenyl)benzoyl]methionine

The desired compound was prepared according to the method of Example 403I starting with compound prepared in Example 1341D. ^1H (300MHz, $CDCl_3$, δ) 7.81 (1H,

d, J=8Hz), 7.57 (1H, m), 7.42 (1H, d, J=2Hz), 7.30-7.10 (5H, m), 6.35 (2H, m), 6.15 (1H, bd, J=8Hz), 4.43 (1H, m), 3.98 (2H, m), 3.90-3.75 (2H, m), 2.62 (2H, m), 2.20-2.00 (5H, m), 1.99 (3H, s), 1.95 (1H, m), 1.60 (3H, m), 1.29 (2H, m), 0.88 (3H, t,
17215 J=8Hz). m/e (ESI) 509 (MH^+) Anal.calc. for $C_{29}H_{36}N_2O_4S \cdot 0.50\ H_2O$ C 67.28, H 7.20, N 5.41 Found C 67.42, H 6.96, N 5.44.

WHAT IS CLAIMED IS:

1. A compound having Formula **I**



I

or a pharmaceutically acceptable salt thereof, wherein

$\mathbf{R_1}$ is selected from the group consisting of

(1) hydrogen,

(2) alkenyl,

(3) alkynyl,

(4) alkoxy,

(5) haloalkyl,

(6) halogen,

(7) loweralkyl,

(8) thioalkoxy,

(9) aryl-L_2- wherein aryl is selected from the group consisting of

(a) phenyl,

(b) naphthyl,

(c) dihydronaphthyl,

(d) tetrahydronaphthyl,

(e) indanyl, and

(f) indenyl

wherein (a)-(f) are unsubstituted or substituted with at least one of X, Y, or Z wherein X, Y, and Z are independently selected from the group consisting of

alkenyl,

alkynyl,

alkoxy,

aryl,

carboxy,

cyano,

halogen,

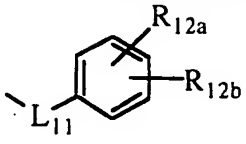
haloalkyl,

hydroxy,
hydroxyalkyl,
loweralkyl,
nitro,
N-protected amino, and
-NRR' wherein R and and R' are independently selected
from the group consisting of
hydrogen and
loweralkyl,
oxo (=O), and
thioalkoxy and

L_2 is absent or is selected from the group consisting of
$-CH_2-$,
$-CH_2CH_2-$,
$-CH(CH_3)-$,
-O-,
-C(O)-,
$-S(O)_q$ wherein q is 0, 1 or 2, and
-N(R)-, and

(10) heterocycle-L_2- wherein L_2 is as defined above and the heterocycle is unsubstituted or substituted with 1, 2, 3 or 4 substituents independently selected from the group consisting of
(a) loweralkyl,
(b) hydroxy,
(c) hydroxyalkyl,
(d) halogen
(e) cyano,
(f) nitro,
(g) oxo (=O),
(h) -NRR',
(i) N-protected amino,
(j) alkoxy,
(k) thioalkoxy,
(l) haloalkyl,
(m) carboxy, and
(n) aryl;

R_2 is selected from the group consisting of

(1)  wherein L_{11} is selected from the group consisting of

(a) a covalent bond,

(b) -C(W)N(R)- wherein R is defined previously and W is selected from the group consisting of O and S,

(c) -C(O)-,

(d) -N(R)C(W)-,

(e) $-CH_2O-$,

(f) -C(O)O-, and

(g) $-CH_2N(R)-$,

R_{12a} is selected from the group consisting of

(a) hydrogen,

(b) loweralkyl, and

(c) $-C(O)OR_{13}$ wherein R_{13} is selected from the group consisting of

hydrogen and

a carboxy-protecting group, and

R_{12b} is selected from the group consisting of

(a) hydrogen and

(b) loweralkyl,

with the proviso that R_{12a} and R_{12b} are not both hydrogen,

(2) $-L_{11}-C(R_{14})(R_v)-C(O)OR_{15}$ wherein L_{11} is defined previously,

R_v is selected from the group consisting of

(a) hydrogen and

(b) loweralkyl,

R_{15} is selected from the group consisting of

(a) hydrogen,

(b) alkanoyloxyalkyl,

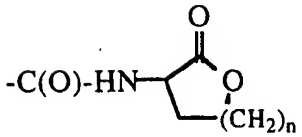
(c) loweralkyl, and

(b) a carboxy-protecting group, and

R_{14} is selected from the group consisting of

(a) alkoxyalkyl,

(b) alkoxyarylalkyl,
(c) alkoxycarbonylalkyl,
(d) alkylsulfinyalkyl,
(e) alkylsulfonylalkyl,
(f) alkynyl,
(g) aminoalkyl,
(h) aminocarbonylalkyl,
(i) aminothiocarbonylalkyl,
(j) aryl,
(k) arylalkyl,
(l) carboxyalkyl,
(m) cyanoalkyl,
(n) cycloalkyl,
(o) cycloalkylalkoxyalkyl,
(p) cycloalkylalkyl,
(q) (heterocyclic)alkyl,
(r) hydroxyalkyl,
(s) hydroxyarylalkyl,
(t) loweralkyl;
(u) sulfhydrylalkyl,
(v) thioalkoxyalkyl wherein the thioalkoxyalkyl is unsubstituted or substituted with 1, 2, 3, or 4 substituents selected from the group consisting of halogen,
(w) thioalkoxyalkylamino, and
(x) thiocycloalkyloxyalkyl,

(3)  wherein n is 1-3,

(4) -C(O)NH-CH(R_{14})-C(O)NHSO_2R_{16} wherein R_{14} is defined previously and R_{16} is selected from the group consisting of
(a) loweralkyl,
(b) haloalkyl,
(c) aryl wherein the aryl is unsubstituted or substituted with

1, 2, 3, 4, or 5 substituents independently selected from the group consisting of
loweralkyl,
hydroxy,
hydroxyalkyl,
halogen,
cyano,
nitro,
oxo (=O),
-NRR'
N-protected amino,
alkoxy,
thioalkoxy,
haloalkyl,
carboxy, and
aryl, and

(d) heterocycle wherein the heterocycle is unsubstituted or substituted with substituents independently selected from the group consisting of
loweralkyl,
hydroxy,
hydroxyalkyl,
halogen,
cyano,
nitro,
oxo (=O),
-NRR',
N-protected amino,
alkoxy,
thioalkoxy,
haloalkyl,
carboxy, and
aryl;

(5) -C(O)NH-CH(R_{14})-tetrazolyl wherein the tetrazole ring is unsubstituted or substituted with loweralkyl or haloalkyl,

(6) -L_{11}-heterocycle,

(7) -C(O)NH-CH(R_{14})-C(O)N$R_{17}R_{18}$ wherein R_{14} is defined previously and R_{17} and R_{18} are independently selected from the group consisting of
(a) hydrogen,
(b) loweralkyl,
(c) arylalkyl,
(d) hydroxy, and
(e) dialkylaminoalkyl,

(8) -C(O)OR_{15}, and

(9) -C(O)NH-CH(R_{14})-heterocycle wherein R_{14} is as previously defined and the heterocycle is unsubstituted or substituted with loweralkyl or haloalkyl;

L_1 is absent or is selected from the group consisting of

(1) -L_4-N(R_5)-L_5- wherein L_4 is absent or selected from the group consisting of
(a) C_1-to-C_{10}-alkylene and
(b) C_2-to-C_{16}-alkenylene,
wherein the alkylene and alkenylene groups are unsubstituted or substituted with 1, 2, 3 or 4 substitutents independently selected from the group consisting of
alkenyl,
alkenyloxy,
alkenyloxyalkyl,
alkenyl[S(O)$_q$]alkyl,
alkoxy,
alkoxyalkyl wherein the alkoxyalkyl is unsubstituted or substituted with 1 or 2 hydroxyl substituents,
with the proviso that no two hydroxyls are attached to the same carbon,
alkoxycarbonyl wherein the alkoxycarbonyl is unsubstituted or substituted with 1, 2, or 3 substituents independently selected from the

group consisting of
halogen and
cycloalkyl,
alkylsilyloxy,
alkyl[$S(O)_q$],
alkyl[$S(O)_q$]alkyl,
aryl wherein the aryl is unsubstituted or substituted with 1, 2, 3, 4, or 5 substituents independently selected from the group consisting of
alkoxy wherein the alkoxy is unsubstituted or substituted with substituents selected from the group consisting of cycloalkyl,
aryl,
arylalkyl,
aryloxy wherein the aryloxy is unsubstituted or substituted with 1, 2, 3, 4, or 5 substituents independently selected from the group consisting of,
halogen,
nitro, and
-NRR',
cycloalkyl,
halogen,
loweralkyl,
hydroxyl,
nitro,
-NRR', and
-SO_2NRR',
arylalkoxy wherein the arylalkoxy is unsubstituted or substituted with substituents selected from the group consisting of alkoxy,
arylalkyl,
arylalkyl[$S(O)_q$]alkyl,
aryl[$S(O)_q$],
aryl[$S(O)_q$]alkyl wherein the aryl[$S(O)_q$]alkyl is unsubstituted or substituted with 1, 2, 3, 4, or 5 substituents independently selected from

alkoxy and
loweralkyl,
arylalkoxyalkyl wherein the arylalkoxyalkyl is unsubstituted or substituted with substituents selected from the group consisting of
alkoxy, and
halogen,
aryloxy,
aryloxyalkyl wherein the aryloxyalkyl is unsubstituted or substituted with substituents selected from the group consisting of halogen,
carboxyl,
-C(O)NR_CR_D wherein R_C and R_D are independently selected from the group consisting of
hydrogen,
loweralkyl, and
alkoxycarbonyl or
R_C and R_D together with the nitrogen to which they are attached form a ring selected from the group consisting of
morpholine,
piperidine,
pyrrolidine
thiomorpholine,
thiomorpholine sulfone, and
thiomorpholine sulfoxide,
wherein the ring formed by R_C and R_D together is unsubstituted or substituted with 1 or 2 substituents independently selected from the group consisting of alkoxy and alkoxyalkyl,
cycloalkenyl wherein the cycloalkenyl is unsubstituted or substituted with 1 or 2 substituents selected from the group consisting of alkenyl,
cyclolalkoxy,
cycloalkoxycarbonyl,

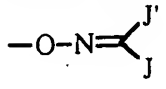
cyclolalkoxyalkyl,
cyclolalkyl wherein the cycloalkyl is unsubstituted or substituted with 1, 2, 3, 4, or 5 substituents independently selected from the group consisting of aryl,
lowеralkyl, and
alkanoyl,
cycloalkylalkoxy,
cycloalkylalkoxycarbonyl,
cycloalkylalkoxyalkyl,
cycloalkylalkyl,
cyclolalkyl[$S(O)_q$]alkyl,
cycloalkylalkyl[$S(O)_q$]alkyl,
fluorenyl,
heterocycle wherein the heterocycle is unsubstituted or substituted with 1, 2, 3, or 4 substituents independently selected from the group consisting of
alkoxy wherein the alkoxy is unsubstituted or substituted with 1 or 2 substituents independently selected from the group consisting of aryl and cycloalkyl,
alkoxyalkyl wherein the alkoxyalkyl is unsubstituted or substituted with 1 or 2 substituents independently selected from the group consisting of
aryl and
cycloalkyl,
alkoxycarbonyl wherein the alkoxycarbonyl is unsubstituted or substituted with 1 or 2 substituents independently selected from the group consisting of
aryl and
cycloalkyl,
aryl wherein the aryl is unsubstituted or substituted with 1, 2, 3, 4, or 5 substituents independently selected from

the group consisting of
alkanoyl,
alkoxy,
carboxaldehyde,
haloalkyl,
halogen,
loweralkyl,
nitro,
-NRR', and
thioalkoxy,
arylalkyl,
aryloxy,
cycloalkoxyalkyl,
cycloalkyl,
cycloalkylalkyl,
halogen,
heterocycle,
hydroxyl,
loweralkyl wherein the loweralkyl is
unsubstituted or substituted with 1, 2, or 3 substituents independently selected from the group consisting of
heterocycle,
hydroxyl,
with the proviso that no two hydroxyls are attached to the same carbon, and
$-NR^{R3R3'}$ wherein R^{R3} and $R^{R3'}$ are independently selected from the group consisting of
hydrogen
aryl,
loweralkyl,
aryl,
arylalkyl,
heterocycle,
(heterocyclic)alkyl,

cycloalkyl, and
cycloalkylalkyl, and
sulfhydryl,
(heterocyclic)alkoxy,
(heterocyclic)alkyl,
(heterocyclic)alkyl[$S(O)_q$]alkyl,
(heterocyclic)oxy,
(heterocyclic)alkoxyalkyl,
(heterocyclic)oxyalkyl,
heterocycle[$S(O)_q$]alkyl,
hydroxyl,
hydroxyalkyl,
imino,
N-protected amino,
=N-O-aryl, and
=N-OH,
=N-O-heterocycle wherein the heterocycle is
unsubstituted or substituted with 1, 2, 3, or 4 substituents independently selected from the group consisting of
loweralkyl,
hydroxy,
hydroxyalkyl,
halogen,
cyano,
nitro,
oxo (=O),
-NRR'
N-protected amino,
alkoxy,
thioalkoxy,
haloalkyl,
carboxy, and
aryl,
=N-O-loweralkyl,
$-NR^{R3}R^{R3'}$,
$-NHNR_CR_D$,

-OG wherein G is a hydroxyl protecting group,

-O-NH-R,



wherein J and J' are independently selected from the group consisting of

loweralkyl and

arylalkyl,

oxo,

oxyamino(alkyl)carbonylalkyl,

oxyamino(arylalkyl)carbonylalkyl,

oxyaminocarbonylalkyl,

$-SO_2$-A wherein A is selected from the group consisting of

loweralkyl,

aryl, and

heterocycle

wherein the loweralkyl, aryl, and heterocycle are unsubstituted or substituted with 1, 2, 3, 4, or 5 substituents independently selected from the group consisting of

alkoxy,

halogen,

haloalkyl,

loweralkyl, and

nitro,

sulfhydryl,

thioxo, and

thioalkoxy,

L_5 is absent or selected from the group consisting of

(a) C_1-to-C_{10}-alkylene and

(b) C_2-to-C_{16}-alkenylene

wherein (a) and (b) are unsubstituted or substituted as defined previously, and

R_5 is selected from the group consisting of

hydrogen,

alkanoyl wherein the alkanoyl is unsubstituted or substituted with substituents selected from the

group consisting of aryl,
alkoxy,
alkoxyalkyl,
alkoxycarbonyl wherein the alkoxycarbonyl is unsubstituted or substituted with 1, 2 or 3 substituents independently selected from the group consisting of
aryl and
halogen,
alkylaminocarbonylalkyl wherein the alkylaminocarbonylalkyl is unsubstituted or substituted with 1 or 2 substituents independently selected from the group consisting of aryl,
(anthracenyl)alkyl,
aryl,
arylalkoxy,
arylalkyl wherein the arylalkyl is unsubstituted or substituted with 1, 2, 3, 4, or 5 substituents independently selected from the group consisting of
alkoxy,
aryl,
carboxyl,
cyano,
halogen,
haloalkoxy,
haloalkyl,
nitro,
oxo, and
$-L_{11}-C(R_{14})(R_v)-C(O)OR_{15}$,
(aryl)oyl wherein the (aryl)oyl is unsubstituted or substituted with substituents selected from the group consisting of halogen,
aryloxycarbonyl,
carboxaldehyde,
-C(O)NRR',

cycloalkoxycarbonyl,
cycloalkylaminocarbonyl,
cycloalkylaminothiocarbonyl,
cyanoalkyl,
cyclolalkyl,
cycloalkylalkyl wherein the cycloalkylalkyl is unsubstituted or substituted with 1 or 2 hydroxyl substituents,
with the proviso that no two hydroxyls are attached to the same carbon,
(cyclolalkyl)oyl,
(9,10-dihydroanthracenyl)alkyl wherein the (9,10-dihydroanthracenyl)alkyl is unsubstituted or substituted with 1 or 2 oxo substituents,
haloalkyl,
heterocycle,
(heterocyclic)alkyl wherein the (heterocyclic)alkyl is unsubstituted or substituted with 1, 2, 3, 4, or 5 substituents selected from the group consisting of loweralkyl,
(heterocyclic)oyl,
loweralkyl, wherein the loweralkyl is unsubstituted or substituted with substituents selected from the group consisting of -NRR',
$-SO_2$-A, and
thioalkoxyalkyl;

(2) $-L_4-O-L_5-$,

(3) $-L_4-S(O)_m-L_5-$ wherein L_4 and L_5 are defined previously and m is 0, 1, or 2,

(4) $-L_4-L_6-C(W)-N(R_6)-L_5-$ wherein L_4, W, and L_5 are defined previously, R_6 is selected from the group consisting of
(a) hydrogen,
(b) loweralkyl,
(c) aryl,

(d) arylalkyl,
(e) heterocycle,
(f) (heterocyclic)alkyl,
(g) cyclolakyl, and
(h) cycloalkylalkyl, and

L_6 is absent or is selected from the group consisting of
(a) -O-,
(b) -S-, and
(c) $-N(R_{6'})-$ wherein $R_{6'}$ is selected from the group consisting of
hydrogen,
loweralkyl,
aryl,
arylalkyl,
heterocycle,
(heterocyclic)alkyl,
cyclolakyl, and
cycloalkylalkyl,

(5) $-L_4-L_6-S(O)_m-N(R_5)-L_5-$,

(6) $-L_4-L_6-N(R_5)-S(O)_m-L_5-$,

(7) $-L_4-N(R_5)-C(W)-L_7-L_5-$ wherein L_4, R_5, W, and and L_5 are defined previously and L_7 is absent or is selected from the group consisting of -O- and -S-,

(8) C_1-C_{10}-alkylene wherein the alkylene group is unsubstituted or substituted with 1 or 2 substituents independently selected from the group consisting of
(a) aryl,
(b) arylalkyl,
(c) heterocycle,
(d) (heterocyclic)alkyl,
(e) cyclolakyl,
(f) cycloalkylalkyl,
(g) alkylthioalkyl, and

(h) hydroxy,

(9) C_2-to-C_{10}-alkenylene wherein the alkenylene group is unsubstituted or substituted with 1 or 2 substituents independently selected from the group consisting of

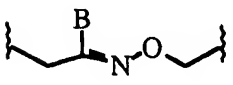
(a) aryl,
(b) arylalkyl,
(c) (aryl)oxyalkyl wherein the (aryl)oxyalkyl is unsubstituted or substituted with 1, 2, 3, 4, or 5 substituents selected from the group consisting of halogen,
(d) heterocycle,
(e) (hererocycle)alkyl,
(f) hydroxyalkyl,
(g) cyclolakyl,
(h) cycloalkylalkyl,
(i) alkylthioalkyl, and
(j) hydroxy,

(10) C_2-to-C_{10}-alkynylene wherein the alkynylene group is unsubstituted or substituted with 1 or 2 substituents independently selected from the group consisting of

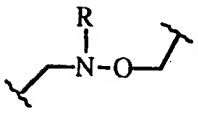
(a) aryl,
(b) arylalkyl,
(c) heterocycle,
(d) (heterocyclic)alkyl,
(e) cyclolakyl,
(f) cycloalkylalkyl,
(g) alkylthioalkyl, and
(h) hydroxy,

(11) -L_4-heterocycle-L_5-,

(12) a covalent bond,

(13)  wherein B is selected from the group consisting of

loweralkyl and
arylalkyl, and

(14)  ;

Z is selected from the group consisting of

(1) a covalent bond,
(2) -O-,
(3) $-S(O)_q-$, and
(4) $-NR_z-$ wherein R_z is selected from the group consisting of
  (a) hydrogen
  (b) loweralkyl,
  (c) aryl,
  (d) arylalkyl,
  (e) heterocycle,
  (f) (heterocyclic)alkyl,
  (g) cyclolakyl, and
  (h) cycloalkylalkyl;

R_3 is selected from the group consisting of

(1) hydrogen,
(2) aryl,
(3) fluorenyl,
(4) heterocycle,

with the proviso that the heterocycle is other than imidazole and pyridine,

wherein (2)-(4) are unsubstituted or substituted with 1, 2, 3, 4, or 5 substituents independently selected from the group consisting of

  (a) alkanoyl,
  (b) alkoxy wherein the alkoxy is unsubstituted or substituted with 1, 2, 3, 4, or 5 substituents independently selected from the group consisting of
    halogen,
    aryl, and
    cycloalkyl,
  (c) alkoxyalkyl wherein the alkoxyalkyl is unsubstituted or substituted with 1 or 2, 3, 4 or 5 substituents

independently selected from the group consisting of
aryl and
cycloalkyl,

(d) alkoxycarbonyl wherein the alkoxycarbonyl is unsubstituted or substituted with 1, 2, 3, 4, or 5 substituents independently selected from the group consisting of
aryl, and
cycloalkyl,

(e) alkylsilyloxyalkyl,

(f) arylalkyl,

(g) aryl wherein the aryl is unsubstituted or substituted with 1, 2, 3, 4, or 5 substituents independently selected from the group consisting of
alkanoyl,
alkoxy wherein the alkoxy is unsubstituted or substituted with 1 or 2 substituents selected from the group consisting of cycloalkyl,
carboxaldehyde,
haloalkyl,
halogen,
loweralkyl,
nitro,
-NRR', and
thioalkoxy,

(h) arylalkyl,

(i) aryloxy wherein the aryloxy is unsubstituted or substituted with 1, 2, 3, 4, or 5 substituents independently selected from the group consisting of,
halogen,
nitro, and
-NRR',

(j) (aryl)oyl,

(k) carboxaldehyde,

(l) carboxy,

(m) carboxyalkyl,

(n) -C(O)NRR" wherein R is defined previously and R" is selected from the group consisting of

hydrogen,
loweralkyl, and
carboxyalkyl,

(o) cyano,

(p) cyanoalkyl,

(q) cycloalkyl,

(r) cycloalkylalkyl,

(s) cycloalkoxyalkyl,

(t) halogen,

(u) haloalkyl wherein the haloalkyl is unsubstituted or substituted with 1, 2, 3, 4, or 5 hydroxyl substituents,
with the proviso that no two hydroxyls are attached to the same carbon,

(v) heterocycle,

(w) hydroxyl,

(x) hydroxyalkyl wherein the hydroxyalkyl is unsubstituted or substituted with substitutients selected from the group consisting of aryl,

(y) loweralkyl wherein the loweralkyl is unsubstituted or substituted with substituents selected from the group consisting of
heterocycle,
hydroxyl,
with the proviso that no two hydroxyls are attached to the same carbon,
$-NR^{R3}R^{R3'}$, and
-P(O)(OR)(OR'),

(z) nitro,

(aa) -NRR',

(bb) oxo,

(cc) $-SO_2NR_{A'}R_{B'}$ wherein $R_{A'}$ and $R_{B'}$ are independently selected from the group consisting of
hydrogen,
(aryl)oyl,
loweralkyl, and
heterocycle wherein the heterocycle is unsubstituted or substituted with 1, 2, or 3 substituents independently selected from the group consisting

of loweralkyl,

(dd) sulfhydryl, and

(ee) thioalkoxy,

(5) cycloalkyl wherein the cycloalkyl is unsubstituted or substituted with 1, 2, 3, 4 or 5 substituents selected from the group consisting of

(a) alkoxy,

(b) aryl,

(c) arylalkoxy

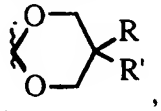
(d) aryloxy wherein the aryloxy is unsubstituted or substituted with 1, 2, 3, 4, or 5 substituents selected from the group consisting of halogen,

(e) loweralkyl,

(f) halogen,

(g) $NR^{R3}R^{R3'}$,

(h) oxo, and

(i)  ,

(6) cycloalkenyl wherein the cycloalkenyl is unsubstituted or substituted with 1, 2, 3 or 4 substituents independently selected from the group consisting of

(a) loweralkyl,

(b) alkoxy,

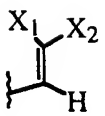
(c) halogen,

(d) aryl,

(e) aryloxy,

(f) alkanoyl, and

(g) $NR^{R3}R^{R3'}$,

(7)  wherein X_1 and X_2 together are cycloalkyl wherein the cycloalkyl is unsubstituted or substituted with 1 or 2 substituents selected from the group consisting of aryl, and

(8) $-P(W)R^{R3}R^{R3'}$; and

R_4 is selected from the group consisting of

(1) hydrogen,

(2) loweralkyl,

(3) haloalkyl

(4) halogen,

(5) aryl,

(6) arylalkyl,

(7) heterocycle,

(8) (heterocyclic)alkyl

(9) alkoxy, and

(10) -NRR'; or

L_1, Z, and R_3 together are selected from the group consisting of

(1) aminoalkyl,

(1) haloalkyl,

(2) halogen,

(3) carboxaldehyde, and

(4) (carboxaldehyde)alkyl, and

(5) hydroxyalkyl,

with the proviso that when L_1, Z, and R_3 together are (1)-(5), R_1 is other than hydrogen.

2. A compound according to claim 1 wherein

L_1 is selected from the group consisting of

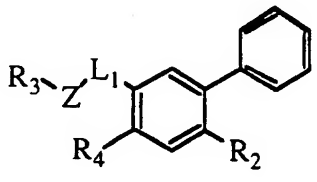
(1) $-L_4-N(R_5)-L_5-$,

(2) $-L_4-L_6-C(W)-N(R_6)-L_5-$, and

(3) $-L_4-N(R_5)-C(W)-L_7-L_5-$ and

Z is a covalent bond or -O-.

3. A compound according to claim 1 of formula



wherein

R_3 is selected from the group consisting of

(1) hydrogen,

(2) aryl,

(3) heterocycle,

(3) fluorenyl,

wherein (2)-(4) are unsubstituted or substituted as defined previously,

(4) cycloalkyl wherein the cycloalkyl is unsubstituted or substituted as defined previously, and

(5) cycloalkenyl wherein the cycloalkenyl is unsubstituted or substituted as defined previously;

L_1 is selected from the group consisting of

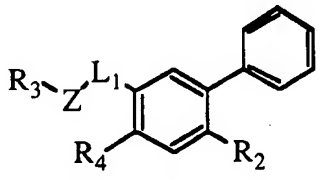
(1) $-L_4-N(R_5)-L_5-$,

(2) $-L_4-L_6-C(W)-N(R_6)-L_5-$, and

(3) $-L_4-N(R_5)-C(W)-L_7-L_5-$; and

Z is a covalent bond or -O-.

4. A compound according to claim 1 of formula



wherein

R_3 is selected from the group consisting of

(1) hydrogen,

(2) aryl,

(3) fluorenyl,

wherein (2) and (3) are unsubstituted or substituted as defined previously,

(4) cycloalkyl wherein the cycloalkyl is unsubstituted or substituted as defined previously, and

(5) cycloalkenyl wherein the cycloalkenyl is unsubstituted or substituted as defined previously;

L_1 is selected from the group consisting of

(1) $-L_4-N(R_5)-L_5-$,

(2) $-L_4-L_6-C(W)-N(R_6)-L_5-$, and

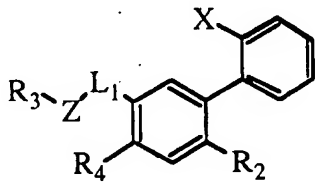
(3) $-L_4-N(R_5)-C(W)-L_7-L_5-$; and

Z is a covalent bond or -O-.

5. A compound according to claim 4 selected from the group consisting of [4-(thiazo-4-ylmethylcarbonyl)amino-2-phenylbenzoyl]methionine, [4-(thiazol-2-ylmethylcarbonyl)amino-2-phenylbenzoyl]methionine, [4-((R)-thiazolidin-4-ylcarbonyl)amino-2-phenylbenzoyl]methionine, methyl ester, hydrochloride, [4-((R)-thiazolidin-4-ylcarbonyl)amino-2-phenylbenzoyl]methionine, [4-((R)-thiazolidin-4-ylmethyl)amino-2-phenylbenzoyl]methionine, hydrochloride, [4-(4-hydroxy-prolinyl)amino-2-phenylbenzoyl]methionine, trifluoroacetate, [4-((2S,4S)-4-mercaptopyrrolidin-2-carboxy)amino-2-phenylbenzoyl]-methionine, trifluoroacetate, [4-((2S,4R)-4-hydroxypyrrolidin-2-ylmethyl)amino-2-phenylbenzoyl]-methionine, hydrochloride, [4-((2S,4S)-4-thiopyrrolidin-2-yl-methylamino)-2-phenylbenzoyl]-methionine, hydrochloride, [4-(1H-benzimidazol-5-ylcarboxyamino)-2-phenylbenzoyl]methionine, trifluoroacetate, [4-(piperidin-2-ylcarboxyamino)-2-phenylbenzoyl]methionine, hydrochloride, [4-(2-pyrrolidinone-5-ylcarbonylamino)-2-phenylbenzoylmethionine, [4-(5-pyrimidylcarboxyamino)-2-phenylbenzoyl]methionine, [4-(3-piperidinecarboxyamino)-2-phenylbenzoyl]methionine, hydrochloride, [4-(1H-4-trifluoromethyl-1,2-dihydropyrid-3-ylcarbonylamino)-2-phenylbenzoyl]methionine, sodium salt, [4-(2-piperazinylmethylamino)-2-phenylbenzoyl]methionine, [4-(2-furylmethylaminomethyl)-2-phenylbenzoyl]methionine lithium salt, N-[4-N-2-hydroxyethylamino-2-phenylbenzoyl]methionine, N-[4-(N-2-amino-3-benzyloxypropionyl)amino-2-phenylbenzoyl]methionine, N-[4-N-phenyl-N-benzylaminomethyl-2-phenylbenzoyl]methionine, N-[4-N-(2-hydroxyethyl)-N-benzylaminomethyl-2-phenylbenzoyl]methionine, lithium salt,

N-[4-N-(t-butylcarbazatocarbonylmethyl)amino-2-phenylbenzoyl]methionine,
N-[4-N,N-dibenzylaminomethyl-2-phenylbenzoyl]methionine, lithium salt,
N-[4-N-(benzyl-N-thiazol-5-ylmethyl)aminomethyl-2-phenylbenzoyl]-methionine,
N-[4-(N-benzylaminomethyl)-2-phenylbenzoyl]methionine, hydrochloride salt,
N-[4-(4-hydroxyprolinylamino)-2-phenylbenzoyl]methionine,
N-[4-((2S,4S)-4-thiolpyrrolidin-2-ylmethylamino)-2-phenylbenzoyl]methionine,
N-[4-((2S,4R)-4-thiolpyrrolidin-2-ylmethylamino)-2-phenylbenzoyl]methionine, and
N-[4-(N-(2-cyclohexylethyl)-N-methylaminomethyl)-2-phenylbenzoyl]-methionine, lithium salt.

6. A compound according to claim 1 of formula



wherein

R_3 is selected from the group consisting of

(1) hydrogen,

(2) aryl,

(3) fluorenyl,

(4) heterocycle

wherein (2)-(4) are unsubstituted or substituted as defined previously,

(5) cycloalkyl wherein the cycloalkyl is unsubstituted or substituted as defined previously, and

(6) cycloalkenyl wherein the cycloalkenyl is unsubstituted or substituted as defined previously;

L_1 is selected from the group consisting of

(1) $-L_4-N(R_5)-L_5-$,

(2) $-L_4-L_6-C(W)-N(R_6)-L_5-$, and

(3) $-L_4-N(R_5)-C(W)-L_7-L_5-$;

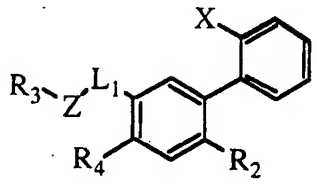
Z is a covalent bond or -O-; and

X is selected from the group consisting of

alkoxy,

aryl,
carboxy,
cyano,
halogen,
haloalkyl,
hydroxy,
hydroxyalkyl,
loweralkyl,
nitro,
N-protected amino,
-NRR,
oxo (=O), and
thioalkoxy.

7. A compound according to claim 1 of formula



wherein

R_3 is selected from the group consisting of

(1) hydrogen,
(2) aryl,
(3) fluorenyl,

wherein (2) and (3) are unsubstituted or substituted as defined previously,

(4) cycloalkyl wherein the cycloalkyl is unsubstituted or substituted as defined previously, and
(5) cycloalkenyl wherein the cycloalkenyl is unsubstituted or substituted as defined previously;

L_1 is selected from the group consisting of

(1) $-L_4-N(R_5)-L_5-$,
(2) $-L_4-L_6-C(W)-N(R_6)-L_5-$, and
(3) $-L_4-N(R_5)-C(W)-L_7-L_5-$;

Z is a covalent bond or -O-; and

X is selected from the group consisting of
alkoxy,
aryl,
carboxy,
cyano,
halogen,
haloalkyl,
hydroxy,
hydroxyalkyl,
loweralkyl,
nitro,
N-protected amino,
-NRR,
oxo (=O), and
thioalkoxy.

8. A compound according to claim 6 wherein X is selected from the group consisting of loweralkyl, halogen, and haloalkyl.

9. A compound according to claim 8 selected from the group consisting of
[4-(1-ethylthio-3-cyclohexylprop-2-ylaminomethyl)-2-(2-methylphenyl)-benzoyl]methionine,
4-(N-benzyl-N-phenyl)-aminomethyl-2-(2-methylphenyl)benzoylmethionine,
N-[4-N-(2,2-dibenzyl-3-hydroxypropyl)amino-2-(2-methylphenyl)benzoyl]-methionine, sodium salt,
N-[4-N-(2-benzyl-3-hydroxypropyl)amino-2-(2-methylphenyl)benzoyl]-methionine, sodium salt,
N-[4-N-(2-cyclohexylmethyl-3-hydroxypropyl)amino-2-(2-methylphenyl)-benzoyl]methionine,
N-[4-N-(furan-2-ylmethyl)-N-benzylaminomethyl-2-(2-methylphenyl)benzoyl]-methionine, lithium salt,
N-[4-N-(2-benzylphenyl)aminomethyl-2-(2-methylphenyl)benzoyl]methionine,
N-[4-N-(2-phenyl)ethyl-N-phenyl)aminomethyl-2-(2-methylphenyl)benzoyl]-methionine,
N-[4-N-(3-phenyl)propyl-N-phenyl)aminomethyl-2-(2-methylphenyl)benzoyl]-methionine,
N-[4-N-(2,2-diphenyl)ethyl-N-phenyl)aminomethyl-2-(2-methylphenyl)-

benzoyl]methionine,
N-[4-N-(adamantan-1-ylmethyl)-N-phenyl)aminomethyl-2-(2-methylphenyl)-benzoyl]methionine,
N-[4-N-(2-adamantan-1-ylethyl)-N-phenyl)aminomethyl-2-(2-methylphenyl)-benzoyl]methionine,
N-[4-N,N-dibenzylaminomethyl-2-(2-methylphenyl)benzoyl]methionine, lithium salt,
N-[4-N-(2-phenylethyl)-N-benzylaminomethyl-2-(2-methylphenyl)benzoyl]-methionine, lithium salt,
N-[4-N-(3-phenoxybenzyl)-N-benzylaminomethyl-2-(2-methylphenyl)-benzoyl]methionine, lithium salt,
N-[4-N-methyl-N-(2-phenyethyl)aminomethyl-2-(2-methylphenyl)benzoyl]-methionine, lithium salt,
N-[4-N-benzyl-N-pyrazin-2-ylaminomethyl-2-(2-methylphenyl)benzoyl]-methionine, lithium salt,
N-[4-N-(2-phenyethyl)-N-pyrimidin-5-ylaminomethyl-2-(2-methylphenyl)-benzoyl]methionine, lithium salt,
N-[4-N-(2-indol-3-ylethyl)aminomethyl-2-(2-methylphenyl)benzoyl]-methionine, lithium salt,
N-[4-N-(2-cyclohexyl-1-ethan-1-ol-2-yl)aminomethyl-2-(2-methylphenyl)-benzoyl]methionine, lithium salt,
N-[4-N-(1,3-diphenylpropan-2-yl)aminomethyl-2-(2-methylphenyl)benzoyl]-methionine, lithium salt,
N-[4-N-(1,3-dicyclohexylpropan-2-yl)aminomethyl-2-(2-methylphenyl)-benzoyl]methionine, lithium salt,
N-[4-N-(1-cyclohexyl-6-methylhept-3-en-2-yl)aminomethyl-2-(2-methyl-phenyl)benzoyl]methionine, lithium salt,
N-[4-N-(1-cyclohexyl-6-methylheptan-2-yl)aminomethyl-2-(2-methylphenyl)-benzoyl]methionine, lithium salt,
N-[4-N-(1-cyclohexyl-2,3-dihydroxy-6-methylheptan-2-yl)aminomethyl-2-(2-methylphenyl)benzoyl]methionine,
N-[4-N-(1-cyclohexyl-2,3-dihydroxy-6-methylheptan-2-yl)aminomethyl-2-(2-methylphenyl)benzoyl]methionine,
N-[4-(3-furan-2-yl-2-phenylprop-2-en-1-ylaminomethyl)-2-(2-methylphenyl)-benzoyl]methionine, lithium salt,
N-[4-(3-furan-2-yl-2-phenylprop-2-en-1-ylaminomethyl)-2-(2-methylphenyl)-benzoyl]methionine, methyl ester,

N-[4-N-phenylacetylamino-2-(2-methylphenyl)benzoyl]methionine, lithium salt,
N-[4-N-(4'-methylphenylacetyl)amino-2-(2-methylphenyl)benzoyl]methionine, lithium salt,
N-[4-N-(4'-methoxyphenylacetyl)amino-2-(2-methylphenyl)benzoyl]-methionine, lithium salt,
N-[4-N-(3-phenylpropionoyl)amino-2-(2-methylphenyl)benzoyl]methionine, lithium salt,
N-[4-N-(3-(2-methoxyphenyl)propionoyl)amino-2-(2-methylphenyl)benzoyl]-methionine, lithium salt,
N-[4-N-benzyl-N-(thiazol-2-ylmethyl)aminomethyl-2-(2-methylphenyl)-benzoyl]methionine,
N-[4-N-benzyl-N-(thiazol-5-ylmethyl)aminomethyl-2-(2-methylphenyl)-benzoyl]methionine,
N-[4-(2-cyclohexylethan-1-ol-2-ylaminomethyl)-2-(2-methylphenyl)benzoyl]-methionine, lithium salt,
N-[4-(N-benzyl-N-(2-cyclohexylethyl)aminomethyl)-2-(2-methylphenyl)-benzoyl]methionine, lithium salt,
N-[4-(N-2-cyclohexylethylaminomethyl)-2-(2-methylphenyl)benzoyl]-methionine, trifluoroacetate salt,
N-[4-(N-(2-cyclohexylethyl)-N-methylaminomethyl)-2-(2-methylphenyl)-benzoyl]methionine, lithium salt,
N-[4-(N-acetyl-N-(2-cyclohexylethyl)aminomethyl)-2-(2-methylphenyl)-benzoyl]methionine, lithium salt,
N-[4-(N-(N,N-dimethylaminocarbonyl)-N-(2-cyclohexylethyl-aminomethyl)-2-(2-methylphenyl)benzoyl]methionine,
N-[4-(N-(2-cyclohexylethyl)-N-methanesulfonylaminomethyl)-2-(2-methylphenyl)benzoyl]methionine, lithium salt,
N-[4-(N-benzenenesulfonyl-N-(2-cyclohexylethyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine lithium salt,
N-[4-(3-cyclohexylpropan-2-ylaminomethyl)-2-(2-methylphenyl)benzoyl]-methionine,
N-[4-(4-cyclohexylbutan-3-ylaminomethyl)-2-(2-methylphenyl)benzoyl]-methionine, lithium salt,
N-[4-(6-cyclohexylhexan-5-ylaminomethyl)-2-(2-methylphenyl)-benzoyl]methionine, lithium salt,
N-[4-(1,2-dicyclohexylethylaminomethyl)-2-(2-methylphenyl)benzoyl]-

methionine, lithium salt,
N-[4-(3-cyclohexylpropan-1-ol-2-ylaminomethyl)-2-(2-methylphenyl)benzoyl]-
95 methionine,
N-[4-(3-cyclohexylpropan-1-ol-2-ylaminomethyl)-2-(2-methylphenyl)benzoyl]-methionine, trifluoroacetate salt,
N-[4-(2-cyclohexylprop-1-en-2-ylaminomethyl)-2-(2-methylphenyl)benzoyl]-methionine, lithium salt,
100 N-[4-(3-cyclohexyl-1-ethylsulfonylpropan-2-ylaminomethyl)-2-(2-methyl-phenyl)benzoyl]methionine, lithium salt,
N-[4-(3-cyclohexyl-1-ethylsulfonylpropan-2-ylaminomethyl)-2-(2-methyl-phenyl)benzoyl]-2-amino-4-methanesulfonylbutanoic acid, lithium salt,
N-[4-(3-cyclohexyl-1-t-butylthiopropan-2-ylaminomethyl)-2-(2-methylphenyl)-
105 benzoyl]methionine, lithium salt,
N-[4-(3-cyclohexyl-1-phenylthiopropan-2-ylaminomethyl)-2-(2-methylphenyl)-benzoyl]methionine, lithium salt,
N-[4-N-benzoyl-N-2-cyclohexylethylaminomethyl-2-(2-methylphenyl)benzoyl]-methionine, lithium salt,
110 N-[4-N-t-butyloxycarbonyl-N-2-cyclohexylethylaminomethyl-2-(2-methyl-phenyl)benzoyl]methionine, lithium salt,
pivaloyloxymethyl N-[4-N-(3-cyclohexyl-1-ethylthiopropan-2-yl)-N-methyl-aminomethyl-2-(2-methylphenyl)benzoyl]methionine, hydrochloride salt,
N-[4-N-(3-cyclohexyl-1-ethylthiopropan-2-yl)-N-methylaminomethyl-2-
115 (2-methylphenyl)benzoyl]-N-methylmethionine, lithium salt,
N-[4-N-(3-cyclohexyl-1-cyclohexylthiopropan-2-yl)-N-methylamino-methyl-2-(2-methylphenyl)benzoyl]methionine, lithium salt,
N-[4-N-(3-cyclohexyl-1-(2-methylphenyl)thiopropan-2-yl)-N-methyl-aminomethyl-2-(2-methylphenyl)benzoyl]methionine, lithium salt,
120 N-[4-N-(N-phenyl-N-benzenesulfonylaminomethyl)-2-(2-methylphenyl)-benzoyl]methionine, lithium salt,
N-[4-N-(N-phenyl-N-toluenesulfonylaminomethyl)-2-(2-methylphenyl)-benzoyl]methionine, lithium salt,
N-[4-N-(N-phenyl-N-(3-methoxybenzyl)aminomethyl)-2-(2-methylphenyl)-
125 benzoyl]methionine, lithium salt,
N-[4-N-(N-phenyl-N-(4-trifluoromethylbenzenesulfonyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine, lithium salt,
N-[4-N-(N-phenyl-N-(4-chlorobenzyl)aminomethyl)-2-(2-methylphenyl)-benzoyl]methionine, lithium salt,

N-[4-N-(N-phenyl-N-(4-trifluoromethylbenzyl)aminomethyl)-2-(2-methylphenyl)-benzoyl]methionine, lithium salt,
N-[4-N(t-butylcarbazatocarbonylmethyl)amino-2-phenylbenzoyl]methionine,
N-[4-(1-ethoxycarbonylpiperidin-4-ylaminomethyl)-2-(2-methylphenyl-benzoyl]methionine, lithium salt,
N-[4-(N-[3-methylthio-1-carboxyprop-2-yl]aminocarbonyl)-2-phenylbenzoyl]-methionine,
N-[4-N-(furan-2-ylmethyl)-N-isopropylaminomethyl-2-(2-methylphenyl)-benzoyl]methionine, lithium salt,
N-[4-N-(furan-3-ylmethyl)-N-isopropylaminomethyl-2-(2-methylphenyl)-benzoyl]methionine, lithium salt,
N-[4-N-benzyl-N-3-methoxyphenylaminomethyl-2-(2-methylphenyl)-benzoyl]methionine, lithium salt,
N-[4-N-(2-phenylethyl)-N-isopropylaminomethyl-2-(2-methylphenyl)-benzoyl]methionine, lithium salt,
N-[4-N-benzyl-N-pyrimidin-5-ylaminomethyl-2-(2-methylphenyl)benzoyl]-methionine, lithium salt,
N-[4-N-(1,3-benzodiox-5-yl)-N-pyrimidin-5-ylaminomethyl-2-(2-methyl-phenyl)benzoyl]methionine, lithium salt,
N-[4-N-(1,3-benzodiox-5-yl)-N-pyridizin-2-ylaminomethyl-2-(2-methylphenyl)-benzoyl]methionine, lithium salt,
N-[4-(N-benzyl-N-(2-methoxyphenyl)aminomethyl)-2-(2-methylphenyl)-benzoyl]methionine, lithium salt,
N-[4-(N-benzyl-N-(4-methoxyphenyl)aminomethyl)-2-(2-methylphenyl)-benzoyl]methionine, lithium salt,
N-[4-(N-benzyl-N-(4-acetylphenyl)aminomethyl)-2-(2-methylphenyl)benzoyl]-methionine, lithium salt,
N-[4-(N-benzyl-N-(3-nitrophenyl)aminomethyl)-2-(2-methylphenyl)benzoyl]-methionine, lithium salt,
N-[4-(N-benzyl-N-(4-nitrophenyl)aminomethyl)-2-(2-methylphenyl)-benzoyl]-methionine, lithium salt,
N-[4-N-(N-benzyl-N-(2-acetylphenyl)aminomethyl)-2-(2-methylphenyl)-benzoyl]methionine, lithium salt,
N-[4-N-(N-benzyl-N-(3-acetylphenyl)aminomethyl)-2-(2-methylphenyl)-benzoyl]methionine, lithium salt,
N-[4-N-(N-benzyl-N-(2-chlorophenyl)aminomethyl)-2-(2-methylphenyl)-benzoyl]methionine, lithium salt,

N-[4-N-(N-benzyl-N-(3-chlorophenyl)aminomethyl)-2-(2-methylphenyl)-benzoyl]methionine, lithium salt,

N-[4-N-(N-benzyl-N-(4-chlorophenyl)aminomethyl)-2-(2-methylphenyl)-benzoyl]methionine, lithium salt,

N-[4-(N-benzyl-N-(2-nitrophenyl)aminomethyl)-2-(2-methylphenyl)benzoyl]-methionine, lithium salt,

N-[4-(N-benzyl-N-(2-methylthiophenyl)aminomethyl)-2-(2-methylphenyl)-benzoyl]methionine, lithium salt,

N-[4-(N-benzyl-N-(3-methylthiophenyl)aminomethyl)-2-(2-methylphenyl)-benzoyl]methionine, lithium salt,

N-[4-(N-benzyl-N-(4-methylthiophenyl)aminomethyl)-2-(2-methylphenyl)-benzoyl]methionine, lithium salt,

N-[4-(N-benzyl-N-(4-trifluoromethylphenyl)aminomethyl)-2-(2-methylphenyl)-benzoyl]methionine, lithium salt,

N-[4-N-(4-piperidin-1-ylphenyl)aminomethyl-2-(2-methylphenyl)benzoyl]-methionine,

N-[4-N-(4-morpholin-1-ylphenyl)aminomethyl-2-(2-methylphenyl)benzoyl]-methionine,

N-[4-N-(4-phenoxyphenyl)aminomethyl-2-(2-methylphenyl)benzoyl]-methionine,

N-[4-N-(benzyl-N-thiazol-2-ylmethyl)aminomethyl-2-(2-methylphenyl)-benzoyl]methionine,

N-[4-N-(toluenesulfonyl-N-thiazol-2-ylmethyl)aminomethyl-2-(2-methyl-phenyl)benzoyl]methionine,

N-[4-N-(methanesulfonyl-N-thiazol-2-ylmethyl)aminomethyl-2-(2-methyl-phenyl)benzoyl]methionine,

N-[4-(N-2-cyclohexylethyl-N-cyclopropylaminomethyl)-2-(2-methylphenyl)-benzoyl]methionine,

N-[4-(N-tetrahydrothiopyran-4-yl-N-thiazol-5-ylaminomethyl)-2-(2-methyl-phenyl)benzoyl]methionine,

N-[4-N-t-butyloxycarbonyl-N-(1,3-dicyclohexylpropan-2-yl)aminomethyl-2-(2-methylphenyl)benzoyl]methionine, lithium salt,

N-[4-N-(3-cyclohexyl-1-oxo-1-piperidin-1-ylpropan-2-yl)aminomethyl-2-(2-methylphenyl)benzoyl]methionine, lithium salt,

N-[4-(N-(1-ethylthio-4-methylpentan-2-yl)aminomethyl)-2-(2-methylphenyl)-benzoyl]methionine,

N-[4-(N-(1-ethylthio-4-methylpentan-2-yl)-N-methylaminomethyl)-2-(2-

methylphenyl)benzoyl]methionine,
N-[4-(N-(1,3-dicyclohexylpropan-2-yl)-N-methylaminomethyl)-2-(2-methylphenyl)benzoyl]methionine,
N-[4-(N-(1,3-dicyclohexylpropan-2-yl)-N-methylaminomethyl)-2-(2-methylphenyl)benzoyl]methionine,
N-[4-(N-acetyl-N-(1,3-dicyclohexylpropan-2-yl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine,
N-[4-(N-benzoyl-N-(1,3-dicyclohexylpropan-2-yl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine,
N-[4-(N-benzenesulfoyl-N-(1,3-dicyclohexylpropan-2-yl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine,
N-[4-(N-(N,N-dibutylacetamido)aminomethyl)-2-(2-methylphenyl)benzoyl]-methionine,
N-[4-(N-(N,N-dibutylacetamido)-N-methylaminomethyl)-2-(2-methylphenyl)-benzoyl]methionine,
N-[4-(N-(N,N-dibenzylacetamido)aminomethyl)-2-(2-methylphenyl)benzoyl]-methionine,
N-[4-(N-(2-cyclohexylethyl)-N-isopropylaminomethyl)-2-(2-methylphenyl)-benzoyl]methionine,
N-[4-(N-butanesulfonyl-N-(2-cyclohexylethyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine,
N-[4-(N,N-dibutylaminomethyl)-2-(2-methylphenyl)benzoyl]methionine,
N-[4-(N-butanesulfonyl-N-(3-phenylpropyl)aminomethyl)-2-(2-methylphenyl)-benzoyl]methionine,
N-[4-(N-butyl-N-(2-phenylethyl)aminomethyl)-2-(2-methylphenyl)benzoyl]-methionine,
N-[4-N-(3-cyclohexyl-1-ethylthiopropan-2-yl)-N-methylaminomethyl-2-(2-methylphenyl)benzoyl]methionine, hydrochloride,
N-[4-N-(3-cyclohexyl-1-ethylthiopropan-2-yl)-N-isobutylaminomethyl-2-(2-methylphenyl)benzoyl]methionine,
N-[4-N-(3-cyclohexyl-1-ethylthiopropan-2-yl)-N-formylaminomethyl-2-(2-methylphenyl)benzoyl]methionine,
N-[4-N-acetyl-N-(3-cyclohexyl-1-ethylthiopropan-2-yl)aminomethyl-2-(2-methylphenyl)benzoyl]methionine,
N-[4-N-t-butyloxycarbonyl-N-(3-cyclohexyl-1-ethylthiopropan-2-yl)amino-methyl-2-(2-methylphenyl)benzoyl]methionine,
N-[4-N-benzoyl-N-(3-cyclohexyl-1-ethylthiopropan-2-yl)aminomethyl-2-(2-

methylphenyl)-benzoyl]methionine,
N-[4-N-butanesulfoyl-N-(3-cyclohexyl-1-ethylthiopropan-2-yl)amino-methyl-2-(2-methylphenyl)benzoyl]methionine,
N-[4-N-benzenesulfonyl-N-(3-cyclohexyl-1-ethylthiopropan-2-yl)amino-methyl-2-(2-methylphenyl)benzoyl]methionine,
N-[4-(N-5-(4-chlorophenyl)furan-2-ylmethyl-N-isopropylaminomethyl)-2-(2-methylphenyl)benzoyl]methionine, lithium salt,
N-[4-(N-methyl-N-(1,1-dimethyl-2-phenylethyl)aminomethyl)-2-(2-methyl-phenyl)benzoyl]methionine, lithium salt,
N-[4-(N-methyl-N-(1,1-dimethyl-2-cyclohexylethyl)aminomethyl)-2-(2-methylphenyl)-benzoyl]methionine, lithium salt,
N-[4-(N-2-cyclohexylethyl-N-thiazol-5-ylmethylaminomethyl)-2-(2-methyl-phenyl)benzoyl]methionine,
N-[4-(1-ethylthio-4-phenylbut-2-oxymethyl)-2-(2-methylphenyl)-benzoyl]-methionine,
N-[4-N-benzyl-N-(4-cyanophenyl)aminomethyl-2-(2-methylphenyl)benzoyl]-methionine, lithium salt,
N-[4-N-benzyl-N-(4-carboxamidophenyl)aminomethyl-2-(2-methylphenyl)-benzoyl]methionine, lithium salt,
N-[4-N-benzyl-N-(4-sulfonamidophenyl)aminomethyl-2-(2-methylphenyl)-benzoyl]methionine, lithium salt,
N-[4-N-benzyl-N-(4-N-benzoylsulfonamidophenyl)aminomethyl-2-(2-methyl-phenyl)benzoyl]methionine, lithium salt,
N-[4-N-benzyl-N-(4-propionylphenyl)aminomethyl-2-(2-methylphenyl)-benzoyl]methionine, lithium salt,
N-[4-N-benzyl-N-(4-benzoylphenyl)aminomethyl-2-(2-methylphenyl)-benzoyl]methionine, lithium salt,
N-[4-N-benzyl-N-(4-(6-methylbenzthiazol-2yl)phenyl)aminomethyl-2-(2-methylphenyl)benzoyl]methionine, lithium salt,
N-[4-N-2,5-difluorobenzyl-N-(4-cyanophenyl)aminomethyl-2-(2-methyl-phenyl)benzoyl]methionine, lithium salt,
N-[4-N-2,4-difluorobenzyl-N-(4-cyanophenyl)aminomethyl-2-(2-methyl-phenyl)benzoyl]methionine, lithium salt,
N-[4-N-3,5-difluorobenzyl-N-(4-cyanophenyl)aminomethyl-2-(2-methyl-phenyl)benzoyl]methionine, lithium salt,
N-[4-N-3,5-difluorobenzyl-N-(4-vinylphenyl)aminomethyl-2-(2-methyl-phenyl)benzoyl]methionine, lithium salt,

N-[4-N-3,5-difluorobenzyl-N-(4-acetylphenyl)aminomethyl-2-(2-methylphenyl)benzoyl]methionine, lithium salt,

N-[4-N-3,5-difluorobenzyl-N-(4-(1-hydroxyethyl)phenyl)aminomethyl-2-(2-methylphenyl)benzoyl]methionine, lithium salt,

N-[4-N-3,5-difluorobenzyl-N-(4-(1-hydroxy-1-phenylmethyl)phenyl)-aminomethyl-2-(2-methylphenyl)benzoyl]methionine, lithium salt,

N-[4-N-3,5-difluorobenzyl-N-(4-(2-hydroxyethyl)phenyl)aminomethyl-2-(2-methylphenyl)benzoyl]methionine, lithium salt,

N-[4-N-3,5-difluorobenzyl-N-(4-(2-tert-butyldimethylsiloxyethyl)phenyl)-aminomethyl-2-(2-methylphenyl)benzoyl]methionine, lithium salt,

N-[4-N-3,5-difluorobenzyl-N-(1-ethylthio-3-cyclohexylprop-2-yl)amino-methyl-2-(2-methylphenyl)benzoyl]methionine,

N-[4-(2-N-piperidin-1-ylaminoethenyl)-2-(2-methylphenyl)benzoyl]methionine, lithium salt,

N-[4-(2-N-2-methoxymethylpyrrolidin-1-ylaminoethenyl)-2-(2-methylphenyl)-benzoyl]methionine, lithium salt,

N-[4-N-(4-trans-pentafluorophenoxycyclohexyl)aminomethyl-2-(2-methylphenyl)benzoyl]methionine,

N-[4-(N-(2-cyclohexylethyl)-N-methylaminomethyl)-2-(2-methylphenyl)-benzoyl]glutamine, trifluoroacetic acid salt,

N-[4-(N-(2-cyclohexylethyl)-N-methylaminomethyl)-2-(2-methylphenyl)-benzoyl]homocysteine, lithium salt,

N-[4-(N-(2-cyclohexylethyl)-N-methylaminomethyl)-2-(2-methylphenyl)-benzoyl]histidine, trifluoroacetic acid salt,

N-[4-(N-cyclohexylmethylaminoethyl)-2-(2-methylphenyl)benzoyl]methionine, lithium salt,

N-[4-(N,N-di-(cyclohexylmethyl)aminoethyl)-2-(2-methylphenyl)benzoyl]-methionine, lithium salt,

N-[4-(N-cyclohexylmethyl-N-phenylacetylaminoethyl)-2-(2-methylphenyl)-benzoyl]methionine, lithium salt,

N-[4-(N-cyclohexylmethyl-N-1-adamantanoylaminoethyl)-2-(2-methylphenyl)-benzoyl]methionine, lithium salt,

N-[4-(N-cyclohexylmethyl-N-t-butoxycarbonylaminoethyl)-2-(2-methylphenyl)-benzoyl]methionine, lithium salt,

N-[4-(N-cyclohexylmethyl-N-2-ethylhexyloxycarbonylaminoethyl)-2-(2-methylphenyl)benzoyl]methionine, lithium salt,

N-[4-(N-cyclohexylmethyl-N-2,2,2-trichloroethoxycarbonylaminoethyl)-2-(2-

methylphenyl)benzoyl]methionine, lithium salt,
N-[4-(N-cyclohexylmethyl-N-cyclohexyloxycarbonylaminoethyl)-2-(2-methyl-phenyl)benzoyl]methionine, lithium salt,
N-[4-(N-cyclohexylmethyl-N-adamantyloxycarbonylaminoethyl)-2-(2-methyl-phenyl)benzoyl]methionine, lithium salt,
N-[4-(N-cyclohexylmethyl-N-phenoxycarbonylaminoethyl)-2-(2-methylphenyl)-benzoyl]methionine, lithium salt,
N-[4-(N-cyclohexylmethyl-N-benzyloxycarbonylaminoethyl)-2-(2-methyl-phenyl)benzoyl]methionine, lithium salt,
N-[4-(N-cyclohexylmethyl-N-adamant-1-aminocarbonylaminoethyl)-2-(2-methylphenyl)benzoyl]methionine, lithium salt,
N-[4-(N-cyclohexylmethyl-N-adamant-1-aminothiocarbonylaminoethyl)-2-(2-methylphenyl)benzoyl]methionine, lithium salt,
N-[4-(N-(2-cyclohexylethyl)-N-methylaminomethyl)-2-(2-methylphenyl)-benzoyl]glutaminitrile, lithium salt,
N-[4-(N-p-toluenesulfonyl-N-methylaminomethyl)-2-(2-methylphenyl)-benzoyl]methionine, lithium salt,
N-[4-(N-(4-benzyloxybenzyl)-N-(N-2-methyl-2-phenylpropylacetamido)-aminomethyl)-2-(2-methylphenyl)benzoyl]methionine, lithium salt,
N-[4-(N-(2-cyclohexenylethyl)-N-methylaminomethyl)-2-(2-methylphenyl)-benzoyl]methionine, lithium salt,
(2S) 2-N-[4-(N-(2-cyclohexylethyl)-N-methylaminomethyl)-2-(2-methyl-phenyl)benzoyl]amino-4-methylsulfenylbutanoate, lithium salt,
(2S) 2-N-[4-(N-(2-cyclohexylethyl)-N-methylaminomethyl)-2-(2-methylphenyl)benzoyl]amino-4-methylsulfonylbutanoate, lithium salt,
N-[4-(N-(2-cyclohexylethyl)-N-methylaminomethyl)-2-(2-methylphenyl)-benzoyl]norleucine, lithium salt,
N-[4-(N-(2-cyclohexylethyl)-N,N-dimethylaminomethyl)-2-(2-methylphenyl)-benzoyl]methionine,
(2S) 2-N-[4-(N-(2-cyclohexylethyl)-N-butylaminomethyl)-2-(2-methylphenyl)-benzoyl]amino-4-methylsulfenylbutanoate, lithium salt,
N-[4-(N-(2-cyclohexylethyl)-N-p-toluenesulfonylaminomethyl)-2-(2-methyl-phenyl)benzoyl]methionine, lithium salt,
N-[4-(N-(2-cyclohexylethyl)-N-m-toluenesulfonylaminomethyl)-2-(2-methyl-phenyl)benzoyl]methionine, lithium salt,
N-[4-(N-(2-cyclohexylethyl)-N-p-tert-butylbenzenesulfonylaminomethyl)-2-(2-methylphenyl)benzoyl]methionine, lithium salt,

N-[4-(N-(2-cyclohexylethyl)-N-p-bromobenzenesulfonylaminomethyl)-2-(2-methylphenyl)benzoyl]methionine, lithium salt,
N-[4-(N-(2-cyclohexylethyl)-N-p-methoxybenzenesulfonylaminomethyl)-2-(2-methylphenyl)benzoyl]methionine, lithium salt,
N-[4-(N-(2-cyclohexylethyl)-N-p-nitrobenzenesulfonylaminomethyl)-2-(2-methylphenyl)benzoyl]methionine, lithium salt,
N-[4-(N-(2-cyclohexyl-2-methylpropyl)-N-methylaminomethyl)-2-(2-methylphenyl)benzoyl]methionine, lithium salt,
N-[4-(3-cyclohexyl-1-methoxyprop-2-ylaminomethyl)-2-(2-methylphenyl)benzoyl]methionine, lithium salt,
N-[4-(1-ethylsulfenyl-3-cyclohexylprop-2-ylaminomethyl)-2-(2-methylphenyl)benzoyl]methionine, lithium salt,
(2S)-2-N-[4-(1-ethylsulfenyl-3-cyclohexylprop-2-ylaminomethyl)-2-(2-methylphenyl)benzoyl]amino-4-methylsulfenylbutanoate, lithium salt,
N-[4-(N-(3-cyclohexylpropyl)-N-benzenesulfonylaminomethyl)-2-(2-methylphenyl)benzoyl]methionine, lithium salt,
N-[4-(N-glucosaminomethyl)-2-(2-methylphenyl)benzoyl]methionine, lithium salt,
(2S)-2-N-[4-(N-2-cyclohexylethyl-N-methylaminomethyl)-2-(2-methylphenyl)benzoyl]amino-4-difluoromethylthiobutanoate, lithium salt,
(2S)-2-N-[4-(N-2-cyclohexylethyl-N-methylaminomethyl)-2-(2-methylphenyl)benzoyl]amino-5-methoxypentanoate, lithium salt,
(2S)-2-N-[4-(N-2-cyclohexylethyl-N-methylaminomethyl)-2-(2-methylphenyl)benzoyl]aminopent-4-ynoate, lithium salt,
2-[4-(N-2-cyclohexylethyl-N-methylaminomethyl)-2-(2-methylphenyl)benzoyl]oxy-4-methylthiobutanoate, lithium salt,
N-[4-(N-(5-bromo-(4-chlorophenyl)furan-2-ylmethyl-N-isopropyl-aminomethyl)-2-(2-methylphenyl)benzoyl]methionine, lithium salt,
N-[4-(N-(5-phenyl-(4-chlorophenyl)furan-2-ylmethyl-N-isopropyl-aminomethyl)-2-(2-methylphenyl)benzoyl]methionine, lithium salt,
N-[4-(N-(5-(3-methoxyphenyl)-(4-chlorophenyl)furan-2-ylmethyl)-N-isopropylaminomethyl)-2-(2-methylphenyl)benzoyl]methionine, lithium salt,
N-[4-(N-(4,5-di(4-chlorophenyl)furan-2-yl)methyl)-N-isopropylamino-methyl)-2-(2-methylphenyl)benzoyl]methionine, lithium salt,
N-[4-(N-(5-thien-3-yl-(4-chlorophenyl)furan-2-yl)methyl)-N-isopropyl-aminomethyl)-2-(2-methylphenyl)benzoyl]methionine, lithium salt,
N-[4-(N-(2-cyclohexylethyl)-N-2-fluoroethylaminomethyl)-2-(2-methyl-

phenyl)benzoyl]methionine,

N-[4-(N-(2-cyclohexylethyl)-N-2,2,2-trifluoroethylaminomethyl)-2-(2-methylphenyl)benzoyl]methionine, lithium salt,

N-[4-(N-(2-cyclohexylethyl)-N-2-methoxyethylaminomethyl)-2-(2-methylphenyl)benzoyl]methionine,

N-[4-(N-(2-cyclohexylethyl)-N-2-methylthioethylaminomethyl)-2-(2-methylphenyl)benzoyl]methionine,

N-[4-(N-(2-cyclohexylethyl)-N-1-methyl-2(S)-methylthioethylaminomethyl)-2-(2-methylphenyl)benzoyl]methionine,

N-[4-(N-(2-cyclohexylethyl)-N-2-N,N-dimethylaminomethyl)-2-(2-methylphenyl)benzoyl]methionine,

N-[4-(N-(1-benzyloxymethyl-2-(S)-ethylthioethylaminomethyl)-2-(2-methylphenyl)benzoyl]methionine,

N-[4-(N-(2-cyclohexylethyl)-N-methylaminomethyl)-2-(2-methylphenyl)-benzoyl]ornithine, trifluoroacetate salt,

N-[4-(N-(2-cyclohexylethyl)-N-2-N-methylaminomethyl)-2-(2-methylphenyl)-benzoyl]thien-2-ylalanine,

N-[4-(1-ethylthio-3-cyclohexylprop-2-ylaminomethyl)-5-fluoro-2-(2-methylphenyl)benzoyl]methionine,

N-[4-(N-butyl-N-4-cyclohexylbenzylaminomethyl)-2-(2-methylphenyl)benzoyl]-methionine, lithium salt,

N-[4-(N-butyl-N-4-cyclohexylbenzoylaminomethyl)-2-(2-methylphenyl)-benzoyl]methionine, lithium salt,

N-[4-(N-cyclohexylaminocarbonylethyl)-2-(2-methylphenyl)benzoyl]-methionine, lithium salt,

N-[4-(N-cyclohexylmethyl-N-butylaminoethyl)-2-(2-methylphenyl)benzoyl]-methionine, lithium salt,

N-[4-(N-cyclohexylmethyl-N-butylaminocarbonylmethyl)-2-(2-methylphenyl)-benzoyl]methionine, lithium salt,

N-[4-(N-cyclohexanoyl-N-butylaminoethyl)-2-(2-methylphenyl)benzoyl]-methionine, lithium salt,

N-[4-(N-cyclohexylmethyl-N-butanoylaminoethyl)-2-(2-methylphenyl)benzoyl]-methionine lithium salt,

N-[4-(N-cyclohexylpropyl)-2-(2-methylphenyl)benzoyl]methionine, lithium salt,

N-[4-(N-cyclohexyl-N-propanoylaminopropyl)-2-(2-methylphenyl)benzoyl]-methionine,

N-[4-(N-cyclohexyl-N-butylaminopropyl)-2-(2-methylphenyl)benzoyl]-

methionine, lithium salt,
N-[4-(N-cyclohexyl-N-methylaminocarbonylethyl)-2-(2-methylphenyl)benzoyl]-methionine, lithium salt,
N-[4-(N-cyclohexyl-N-butylaminocarbonylethyl)-2-(2-methylphenyl)benzoyl]-methionine, lithium salt,
N-[4-(N,N-dicyclohexylaminocarbonylethyl)-2-(2-methylphenyl)benzoyl]-methionine, lithium salt,
N-[4-(N-adamant-1-ylaminocarbonylethyl)-2-(2-methylphenyl)benzoyl]-methionine, lithium salt,
N-[4-(N-adamant-2-ylaminocarbonylethyl)-2-(2-methylphenyl)benzoyl]-methionine, lithium salt,
N-[4-(N-adamant-1-ylmethylaminocarbonylethyl)-2-(2-methylphenyl)benzoyl]-methionine, lithium salt,
N-[4-(N-mytanylmethylaminocarbonylethyl)-2-(2-methylphenyl)benzoyl]-methionine, lithium salt,
N-[4-(N-cyclooctanylaminocarbonylethyl)-2-(2-methylphenyl)-benzoyl]-methionine, lithium salt,
3-[4-(N-cyclohexyl-N-methylaminomethyl)-2-(2-methylphenyl)benzoylmethyl]-4-methylthiobutyric acid,
N-[4-(N-butylaminocarbonylmethyl)-2-(2-methylphenyl)benzoyl]methionine, lithium salt,
N-[4-(N-(2,2,4,4-tetramethylbutylamino)carbonylethyl)-2-(2-methylphenyl)-benzoyl]methionine, lithium salt,
N-[4-(N,N-dibutylaminopropyl)-2-(2-methylphenyl)benzoyl]methionine, lithium salt,
N-[4-N-(2-ethylphenyl)aminomethyl-2-(2-methylphenyl)benzoyl]methionine,
N-[4-N-(2-propylphenyl)aminomethyl-2-(2-methylphenyl)benzoyl]methionine,
N-[4-N-(2-butylphenyl)aminomethyl-2-(2-methylphenyl)benzoyl]methionine,
N-[4-N-(4-butylphenyl)aminomethyl-2-(2-methylphenyl)benzoyl]methionine,
N-[4-N-(2-butylphenyl)-N-(3,5-difluorobenzyl)aminomethyl-2-(2-methyl-phenyl)benzoyl]methionine,
N-[4-N-(2,6-diethylphenyl)-N-(3,5-difluorobenzyl)aminomethyl-2-(2-methyl-phenyl)benzoyl]methionine, lithium salt,
N-[4-N-(2-butylphenyl)-N-(cyclohexylmethyl)aminomethyl-2-(2-methylphenyl)-benzoyl]methionine, lithium salt,
N-[4-N-(2-cyclohexylethyl)-N-(3-methylphenyl)aminomethyl-2-(2-methyl-phenyl)benzoyl]methionine,

N-[4-N-(2-butylphenyl)-N-(2-cyclohexylethyl)aminomethyl-2-(2-methylphenyl)benzoyl]methionine,

N-[4-N-butyl-N-(2-(3,5-difluoro)phenylethyl)aminomethyl-2-(2-methylphenyl)-benzoyl]methionine,

N-[4-N-butanesulfonyl-N-(2-phenylethyl)aminomethyl-2-(2-methylphenyl)-benzoyl]methionine lithium salt,

N-[4-N-(2-cyclohexylethyl)-N-methylaminomethyl-2-(2-methylphenyl)-benzoyl]-3-aminotetrahydrofuran-2-one,

N-[4-(N-(-2-cyclohexylethyl)-N-butylaminomethyl)-2-(2-methylphenyl)-benzoyl]methionine, lithium salt,

N-[4-N-butyl-N-(2-cyclohexylethyl)aminomethyl-2-(2-methylphenyl)benzoyl]-methionine 4-methylphenylsulfonimide,

N-[4-N-butyl-N-(1-phenyltetrazol-5-yl)aminomethyl-2-(2-methylphenyl)-benzoyl]methionine,

N-[4-N-t-butyl-N-(2-cyclohexylethyl)aminomethyl-2-(2-methylphenyl)-benzoyl]methionine,

N-[4-N-(2-cyclohexylethyl)-N-(pent-2-yl)aminomethyl-2-(2-methylphenyl)-benzoyl]methionine,

N-[4-N-(2-cyclohexylethyl)-N-(pent-2-yl)aminomethyl-2-(2-methylphenyl)-benzoyl]methionine,

N-[4-N-(2-cyclohexylethyl)-N-propyloxyaminomethyl-2-(2-methylphenyl)-benzoyl]methionine, lithium salt,

N-[4-N-(2-cyclohexylethyl)-N-propanesulfonylaminomethyl-2-(2-methylphenyl)benzoyl]methionine,

N-[4-N-(3-chloropropanesulfonyl)-N-(2-cyclohexylethyl)aminomethyl-2-(2-methylphenyl)benzoyl]methionine,

N-[4-N-(2-cyclohexylethyl)-N-(3-ethoxypropanesulfonyl)aminomethyl-2-(2-methylphenyl)benzoyl]methionine lithium salt,

N-[4-N-(2-cyclohexylethyl)-N-(3-trifluoromethylpropanesulfonyl)amino-methyl-2-(2-methylphenyl)benzoyl]methionine,

N-[4-N-(butanesulfonyl)-N-(3-cyclohexylpropyl)aminomethyl-2-(2-methylphenyl)benzoyl]methionine, lithium salt,

N-[4-N-(4-cyclohexyl-1-ethylthiobutan-2-yl)aminomethyl-2-(2-methylphenyl)-benzoyl]methionine,

N-[4-N-(butanesulfonyl)-N-(4-cyclohexylbutyl)aminomethyl-2-(2-methylphenyl)benzoyl]methionine, lithium salt,

N-[4-N-butyl-N-quinolin-2-ylaminomethyl-2-(2-methylphenyl)benzoyl]-

methionine,
N-[4-(N-butyl-N-(2-piperidin-1-ylethyl)aminomethyl)-2-(2-methylphenyl)-benzoyl]methionine,
N-[4-N-((1-norpholinocarbonyl)butyl)aminomethyl-2-(2-methylphenyl)-benzoyl]methionine,
N-[4-N-butyl-N-(2-morpholin-4-ylethyl)aminomethyl-2-(2-methylphenyl)-benzoyl]methionine,
N-[4-N-butyl-N-(fluoren-9-yl)aminomethyl-2-(2-methylphenyl)benzoyl]-methionine,
N-[4-N-(2-cyclohexylethyl)-N-(furan-2-ylmethyl)aminomethyl-2-(2-methyl-henyl)benzoyl]methionine,
N-[4-N-butyl-N-(2-pyrrolidin-1-ylethyl)aminomethyl-2-(2-methylphenyl)-benzoyl]methionine,
N-[4-N-(2-butylphenyl)-N-(thiazol-5-ylmethyl)aminomethyl-2-(2-methyl-phenyl)benzoyl]methionine,
N-[4-N-((2-ethylthio)-1,3,4-thiadiazol-5-yl)aminomethyl-2-(2-methylphenyl)-benzoyl]methionine,
N-[4-N-butyl-N-((2-ethylthio)-1,3,4-thiadiazol-5-yl)aminomethyl-2-(2-methyl-phenyl)benzoyl]methionine,
N-[4-(N-butyl-N-(2-phenylethyl)aminomethyl)-2-(2-methylphenyl)benzoyl]-methionine p-tolylsulfonimide, hydrochloride salt,
N-[4-(N-butyl-N-(2-phenylethyl)aminomethyl)-2-(2-methylphenyl)-benzoyl]methionine 4-(aminomethyl)phenylsulfonimide, dihydrochloride salt,
N-[4-(N-butyl-N-(2-phenylethyl)aminomethyl)-2-(2-methylphenyl)-benzoyl]methionine, isopropylsulfonimide,
N-[4-N-(N-phenyl-N-(4-fluorobenzoyl)aminomethyl)-2-(2-methylphenyl)-benzoyl]methionine, lithium salt,
N-[4-N-(N-phenyl-N-(n-butanesulfonyl)aminomethyl)-2-(2-methylphenyl)-benzoyl]methionine, lithium salt,
N-[4-N-(N-phenyl-N-(3-nitrobenzenesulfonyl)aminomethyl)-2-(2-methyl-phenyl)benzoyl]methionine, lithium salt,
N-[4-N-(N-phenyl-N-(4-fluorobenzenesulfonyl)aminomethyl)-2-(2-methyl-phenyl)benzoyl]methionine, lithium salt,
N-[4-N-(N-phenyl-N-(4-ethylbenzenesulfonyl)aminomethyl)-2-(2-methyl-phenyl)benzoyl]methionine, lithium salt,
N-[4-N-(N-phenyl-N-(4-nitrobenzenesulfonyl)aminomethyl)-2-(2-methyl-phenyl)benzoyl]methionine, lithium salt,

N-[4-N-(N-phenyl-N-(2,3-dichlorobenzenesulfonyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine, lithium salt,
N-[4-N-(N-3,4-(methylenedioxy)phenyl-N-(4-fluorobenzyl)-aminomethyl)-2-(2-methylphenyl)benzoyl]methionine, lithium salt,
N-[4-N-(N-3,4-(methylenedioxy)phenyl-N-(4-fluorobenzyl)-aminomethyl)-2-(2-methylphenyl)benzoyl]methionine, lithium salt,
N-[4-N-(N-phenyl-N-(2-fluorobenzyl)aminomethyl)-2-(2-methylphenyl)-benzoyl]methionine, lithium salt,
N-[4-N-(N-phenyl-N-(3-fluorobenzyl)aminomethyl)-2-(2-methylphenyl)-benzoyl]methionine, lithium salt,
N-[4-N-(N-phenyl-N-(4-fluorobenzyl)aminomethyl)-2-(2-methylphenyl)-benzoyl]methionine, lithium salt,
N-[4-N-(N-phenyl-N-(4-bromobenzyl)aminomethyl)-2-(2-methylphenyl)-benzoyl]methionine, lithium salt,
N-[4-N-(N-phenyl-N-(4-cyanobenzyl)aminomethyl)-2-(2-methylphenyl)-benzoyl]methionine, lithium salt,
N-[4-N-(N-phenyl-N-(4-methoxybenzyl)aminomethyl)-2-(2-methylphenyl)-benzoyl]methionine, lithium salt,
N-[4-N-(N-phenyl-N-(4-trifluoromethoxybenzyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine, lithium salt,
N-[4-N-(N-phenyl-N-(4-nitrobenzyl)aminomethyl)-2-(2-methylphenyl)-benzoyl]methionine, lithium salt,
N-[4-N-(N-phenyl-N-(4-carboxylic acid benzyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine, dilithium salt,
N-[4-N-(N-phenyl-N-(4-phenylbenzyl)aminomethyl)-2-(2-methylphenyl)-benzoyl]methionine, lithium salt,
N-[4-N-(N-phenyl-N-(4-N-carboxymethionine)benzyl)aminomethyl-2-(2-methylphenyl)benzoyl]methionine, dilithium salt,
N-[4-N-(N-phenyl-N-(2-naphthyl)aminomethyl)-2-(2-methylphenyl)-benzoyl]methionine, lithium salt,
N-[4-N-(N-phenyl-N-(9-methyl-anthracene-yl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine, lithium salt,
N-[4-N-(N-phenyl-N-(2-methyl-anthraquinone-yl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine, lithium salt,
N-[4-N-(N-phenyl-N-(2,3-difluorobenzyl)aminomethyl)-2-(2-methylphenyl)-benzoyl]methionine, lithium salt,
N-[4-N-(N-phenyl-N-(2,4-difluorobenzyl)aminomethyl)-2-(2-methylphenyl)-

benzoyl]methionine, lithium salt,
N-[4-N-(N-phenyl-N-(2-thiophenesulfonyl)aminomethyl)-2-(2-methylphenyl)-benzoyl]methionine, lithium salt,
N-[4-N-(N-phenyl-N-(2-methyl-4-methylemethiazolyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine, lithium salt,
N-[4-N-(N-3,5-difluorophenyl-N-(5-thiazolylmethyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine, lithium salt,
N-[4-N-(N-(5-thiazolylmethyl)-N-(3,5-difluorobenzyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine, lithium salt,
N-[4-N-(N-phenyl-N-(3,5-difluorobenzyl)aminomethyl)-2-(2-methylphenyl)-benzoyl]methionine, lithium salt,
N-[4-N-(N-(4-acetonitrilephenyl-N-(3,5-difluorobenzyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine, lithium salt,
N-[4-N-(N-phenyl-N-(3-methoxy-5-nitrobenzyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine, lithium salt,
N-[4-N-(N-(4-nitrophenyl-N-(4-methoxybenzyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine, lithium salt,
N-[4-N-(N-butyl-N-(3,5-difluorobenzyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine, lithium salt,
N-[4-N-(N-(4,4,4-trifluorobutyl-N-(3,5-difluorobenzyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine, lithium salt,
N-[4-N-(N-cyclohexyl-N-(3,5-difluorobenzyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine, lithium salt,
N-[4-N-(N-(4-cyclohexanonyl)-N-(3,5-difluorobenzyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine, lithium salt,
N-[4-N-(N-(4-(2,2-dimethyltrimethylene ketal)-cyclohexyl)-N-(3,5-difluorobenzyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine, lithium salt,
N-[4-N-(N-cyclohexylmethyl-N-(2,4-difluorobenzyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine, lithium salt,
N-[4-N-(N-cyclohexylmethyl-N-(3,5-difluorobenzyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine, lithium salt,
N-[4-N-(N-(4-cyanobenzyl)-N-(3,5-difluorobenzyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine, lithium salt,
N-[4-N-(N-(3,5-difluorobenzyl)-N-(4-N-carboxymethionine)benzyl)-aminomethyl-2-(2-methylphenyl)benzoyl]methionine, dilithium salt,
N-[4-N-(N-(2-cyclohexylethyl-N-(3,5-difluorobenzyl)aminomethyl)-2-

(2-methylphenyl)benzoyl]methionine, lithium salt,
N-[4-N-(N-(3-methylthiopropyl)-N-(3,5-difluorobenzyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine, lithium salt,
N-[4-N-(N-cyclopropyl-N-(2-(3,5-difluorophenyl)ethyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine, lithium salt,
[4-N-(N-2-methylbutyl-N-(2-(2,4-difluorophenyl)ethyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine, lithium salt,
[4-N-(N-butyl-N-(2-(2,4-difluorophenyl)ethyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine, lithium salt,
N-[4-N-(N-(4-methyltetrahydropyran-yl)-N-(3,5-difluorobenzyl)-aminomethyl)-2-(2-methylphenyl)benzoyl]methionine, lithium salt,
N-[4-N-(N-(4-methyltetrahydrothiopyran-yl)-N-(3,5-difluorobenzyl)-aminomethyl)-2-(2-methylphenyl)benzoyl]methionine, lithium salt,
N-[4-N-(N-(4-tetrahydropyran-yl)-N-(3,5-difluorobenzyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine, lithium salt,
N-[4-(N-(3-cyclohexyl-1-ethylthioprop-2-yl)aminomethyl)-2-(2-methylphenyl)benzoyl]amino-4-methylsulfonylbutanoate, lithium salt,
N-[4-(N-methyl-N-(2-cyclohexylethyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine, p-tolylsulfonimide,
N-[4-N-(N-(trans-4-hydroxycyclohexyl)-N-(3,5-difluorobenzyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine, lithium salt,
N-[4-N-(N-(cis-4-hydroxycyclohexyl)-N-(3,5-difluorobenzyl)-aminomethyl)-2-(2-methylphenyl)benzoyl]methionine, lithium salt,
(2S) 2-N-[4-(1-ethylthio-3-cyclohexylprop-2-ylaminomethyl)-2-(2-methylphenyl)benzoyl]amino-4-methylsulfenylbutanoate, lithium salt,
N-[4-(N-(2-(1,3-dioxan-2-ylethyl)-N-butylaminomethyl)-2-(2-methylphenyl)-benzoyl]methionine,
N-[4-(N-(2-cyclohexylethyl)-N-methylaminomethyl)-2-(2-methylphenyl)-benzoyl]thioglutamine, lithium salt,
N-[4-(1-ethylthio-3-cyclohexylprop-2-ylaminomethyl)-5-methoxy-2-(2-methylphenyl)benzoyl]methionine,
N-[4-(1-ethylthio-3-cyclohexylprop-2-ylaminomethyl)-5-N'N'-dimethyl-amino-2-(2-methylphenyl)benzoyl]methionine,
N-[4-N-(6-fluorobenzothiazol-2-yl)aminomethyl-2-(2-methylphenyl)-benzoyl]methionine, and
N-[4-N-butyl-N-(furan-2-ylmethyl)aminomethyl-2-(2-methylphenyl)benzoyl]-methionine.

10. A compound selected from the group consisting of
[4-(thiazo-4-ylmethylcarbonyl)amino-2-phenylbenzoyl]methionine,
[4-(thiazol-2-ylmethylcarbonyl)amino-2-phenylbenzoyl]methionine,
[4-((R)-thiazolidin-4-ylcarbonyl)amino-2-phenylbenzoyl]methionine,
methyl ester, hydrochloride,
[4-((R)-thiazolidin-4-ylcarbonyl)amino-2-phenylbenzoyl]methionine,
[4-((R)-thiazolidin-4-ylmethyl)amino-2-phenylbenzoyl]methionine,
hydrochloride,
[4-(4-hydroxy-prolinyl)amino-2-phenylbenzoyl]methionine, trifluoroacetate,
[4-((2S,4S)-4-mercaptopyrrolidin-2-carboxy)amino-2-phenylbenzoyl]-
methionine, trifluoroacetate,
[4-((2S,4R)-4-hydroxypyrrolidin-2-ylmethyl)amino-2-phenylbenzoyl]-
methionine, hydrochloride,
[4-((2S,4S)-4-thiopyrrolidin-2-yl-methylamino)-2-phenylbenzoyl]-methionine,
hydrochloride,
[4-(1H-benzimidazol-5-ylcarboxyamino)-2-phenylbenzoyl]methionine,
trifluoroacetate,
[4-(piperidin-2-ylcarboxyamino)-2-phenylbenzoyl]methionine,
hydrochloride,
[4-(2-pyrrolidinone-5-ylcarbonylamino)-2-phenylbenzoylmethionine,
[4-(5-pyrimidylcarboxyamino)-2-phenylbenzoyl]methionine,
[4-(3-piperidinecarboxyamino)-2-phenylbenzoyl]methionine,
hydrochloride,
[4-(1H-4-trifluoromethyl-1,2-dihydropyrid-3-ylcarbonylamino)-2-
phenylbenzoyl]methionine, sodium salt,
[4-(2-piperazinylmethylamino)-2-phenylbenzoyl]methionine,
[4-(2-furylmethylaminomethyl)-2-phenylbenzoyl]methionine lithium salt,
N-[4-N-2-hydroxyethylamino-2-phenylbenzoyl]methionine,
N-[4-(N-2-amino-3-benzyloxypropionyl)amino-2-phenylbenzoyl]methionine,
N-[4-N-phenyl-N-benzylaminomethyl-2-phenylbenzoyl]methionine,
N-[4-N-(2-hydroxyethyl)-N-benzylaminomethyl-2-
phenylbenzoyl]methionine, lithium salt,
N-[4-N-(t-butylcarbazatocarbonylmethyl)amino-2-phenylbenzoyl]methionine,
N-[4-N,N-dibenzylaminomethyl-2-phenylbenzoyl]methionine, lithium salt,
N-[4-N-(benzyl-N-thiazol-5-ylmethyl)aminomethyl-2-phenylbenzoyl]-
methionine,

N-[4-(N-benzylaminomethyl)-2-phenylbenzoyl]methionine, hydrochloride salt,
N-[4-(4-hydroxyprolinylamino)-2-phenylbenzoyl]methionine,
N-[4-((2S,4S)-4-thiolpyrrolidin-2-ylmethylamino)-2-phenylbenzoyl]methionine,
N-[4-((2S,4R)-4-thiolpyrrolidin-2-ylmethylamino)-2-phenylbenzoyl]methionine,
N-[4-(N-(2-cyclohexylethyl)-N-methylaminomethyl)-2-phenylbenzoyl]-methionine, lithium salt,
[4-(1-ethylthio-3-cyclohexylprop-2-ylaminomethyl)-2-(2-methylphenyl)-benzoyl]methionine,
4-(N-benzyl-N-phenyl)-aminomethyl-2-(2-methylphenyl)benzoylmethionine,
N-[4-N-(2,2-dibenzyl-3-hydroxypropyl)amino-2-(2-methylphenyl)benzoyl]-methionine, sodium salt,
N-[4-N-(2-benzyl-3-hydroxypropyl)amino-2-(2-methylphenyl)benzoyl]-methionine, sodium salt,
N-[4-N-(2-cyclohexylmethyl-3-hydroxypropyl)amino-2-(2-methylphenyl)-benzoyl]methionine,
N-[4-N-(furan-2-ylmethyl)-N-benzylaminomethyl-2-(2-methylphenyl)benzoyl]-methionine, lithium salt,
N-[4-N-(2-benzylphenyl)aminomethyl-2-(2-methylphenyl)benzoyl]methionine,
N-[4-N-(2-phenyl)ethyl-N-phenyl)aminomethyl-2-(2-methylphenyl)benzoyl]-methionine,
N-[4-N-(3-phenyl)propyl-N-phenyl)aminomethyl-2-(2-methylphenyl)benzoyl]-methionine,
N-[4-N-(2,2-diphenyl)ethyl-N-phenyl)aminomethyl-2-(2-methylphenyl)-benzoyl]methionine,
N-[4-N-(adamantan-1-ylmethyl)-N-phenyl)aminomethyl-2-(2-methylphenyl)-benzoyl]methionine,
N-[4-N-(2-adamantan-1-ylethyl)-N-phenyl)aminomethyl-2-(2-methylphenyl)-benzoyl]methionine,
N-[4-N,N-dibenzylaminomethyl-2-(2-methylphenyl)benzoyl]methionine, lithium salt,
N-[4-N-(2-phenylethyl)-N-benzylaminomethyl-2-(2-methylphenyl)benzoyl]-methionine, lithium salt,
N-[4-N-(3-phenoxybenzyl)-N-benzylaminomethyl-2-(2-methylphenyl)-benzoyl]methionine, lithium salt,
N-[4-N-methyl-N-(2-phenyethyl)aminomethyl-2-(2-methylphenyl)benzoyl]-methionine, lithium salt,
N-[4-N-benzyl-N-pyrazin-2-ylaminomethyl-2-(2-methylphenyl)benzoyl]-

methionine, lithium salt,
N-[4-N-(2-phenyethyl)-N-pyrimidin-5-ylaminomethyl-2-(2-methylphenyl)-benzoyl]methionine, lithium salt,
N-[4-N-(2-indol-3-ylethyl)aminomethyl-2-(2-methylphenyl)benzoyl]-methionine, lithium salt,
N-[4-N-(2-cyclohexyl-1-ethan-1-ol-2-yl)aminomethyl-2-(2-methylphenyl)-benzoyl]methionine, lithium salt,
N-[4-N-(1,3-diphenylpropan-2-yl)aminomethyl-2-(2-methylphenyl)benzoyl]-methionine, lithium salt,
N-[4-N-(1,3-dicyclohexylpropan-2-yl)aminomethyl-2-(2-methylphenyl)-benzoyl]methionine, lithium salt,
N-[4-N-(1-cyclohexyl-6-methylhept-3-en-2-yl)aminomethyl-2-(2-methyl-phenyl)benzoyl]methionine, lithium salt,
N-[4-N-(1-cyclohexyl-6-methylheptan-2-yl)aminomethyl-2-(2-methylphenyl)-benzoyl]methionine, lithium salt,
N-[4-N-(1-cyclohexyl-2,3-dihydroxy-6-methylheptan-2-yl)aminomethyl-2-(2-methylphenyl)benzoyl]methionine,
N-[4-N-(1-cyclohexyl-2,3-dihydroxy-6-methylheptan-2-yl)aminomethyl-2-(2-methylphenyl)benzoyl]methionine,
N-[4-(3-furan-2-yl-2-phenylprop-2-en-1-ylaminomethyl)-2-(2-methylphenyl)-benzoyl]methionine, lithium salt,
N-[4-(3-furan-2-yl-2-phenylprop-2-en-1-ylaminomethyl)-2-(2-methylphenyl)-benzoyl]methionine, methyl ester,
N-[4-N-phenylacetylamino-2-(2-methylphenyl)benzoyl]methionine, lithium salt,
N-[4-N-(4'-methylphenylacetyl)amino-2-(2-methylphenyl)benzoyl]methionine, lithium salt,
N-[4-N-(4'-methoxyphenylacetyl)amino-2-(2-methylphenyl)benzoyl]-methionine, lithium salt,
N-[4-N-(3-phenylpropionoyl)amino-2-(2-methylphenyl)benzoyl]methionine, lithium salt,
N-[4-N-(3-(2-methoxyphenyl)propionoyl)amino-2-(2-methylphenyl)benzoyl]-methionine, lithium salt,
N-[4-N-benzyl-N-(thiazol-2-ylmethyl)aminomethyl-2-(2-methylphenyl)-benzoyl]methionine,
N-[4-N-benzyl-N-(thiazol-5-ylmethyl)aminomethyl-2-(2-methylphenyl)-benzoyl]methionine,

N-[4-(2-cyclohexylethan-1-ol-2-ylaminomethyl)-2-(2-methylphenyl)benzoyl]-methionine, lithium salt,
N-[4-(N-benzyl-N-(2-cyclohexylethyl)aminomethyl)-2-(2-methylphenyl)-benzoyl]methionine, lithium salt,
N-[4-(N-2-cyclohexylethylaminomethyl)-2-(2-methylphenyl)benzoyl]-methionine, trifluoroacetate salt,
N-[4-(N-(2-cyclohexylethyl)-N-methylaminomethyl)-2-(2-methylphenyl)-benzoyl]methionine, lithium salt,
N-[4-(N-acetyl-N-(2-cyclohexylethyl)aminomethyl)-2-(2-methylphenyl)-benzoyl]methionine, lithium salt,
N-[4-(N-(N,N-dimethylaminocarbonyl)-N-(2-cyclohexylethyl-aminomethyl)-2-(2-methylphenyl)benzoyl]methionine,
N-[4-(N-(2-cyclohexylethyl)-N-methanesulfonylaminomethyl)-2-(2-methylphenyl)benzoyl]methionine, lithium salt,
N-[4-(N-benzenenesulfonyl-N-(2-cyclohexylethyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine lithium salt,
N-[4-(3-cyclohexylpropan-2-ylaminomethyl)-2-(2-methylphenyl)benzoyl]-methionine,
N-[4-(4-cyclohexylbutan-3-ylaminomethyl)-2-(2-methylphenyl)benzoyl]-methionine, lithium salt,
N-[4-(6-cyclohexylhexan-5-ylaminomethyl)-2-(2-methylphenyl)-benzoyl]methionine, lithium salt,
N-[4-(1,2-dicyclohexylethylaminomethyl)-2-(2-methylphenyl)benzoyl]-methionine, lithium salt,
N-[4-(3-cyclohexylpropan-1-ol-2-ylaminomethyl)-2-(2-methylphenyl)benzoyl]-methionine,
N-[4-(3-cyclohexylpropan-1-ol-2-ylaminomethyl)-2-(2-methylphenyl)benzoyl]-methionine, trifluoroacetate salt,
N-[4-(2-cyclohexylprop-1-en-2-ylaminomethyl)-2-(2-methylphenyl)benzoyl]-methionine, lithium salt,
N-[4-(3-cyclohexyl-1-ethylsulfonylpropan-2-ylaminomethyl)-2-(2-methyl-phenyl)benzoyl]methionine, lithium salt,
N-[4-(3-cyclohexyl-1-ethylsulfonylpropan-2-ylaminomethyl)-2-(2-methyl-phenyl)benzoyl]-2-amino-4-methanesulfonylbutanoic acid, lithium salt,
N-[4-(3-cyclohexyl-1-t-butylthiopropan-2-ylaminomethyl)-2-(2-methylphenyl)-benzoyl]methionine, lithium salt,
N-[4-(3-cyclohexyl-1-phenylthiopropan-2-ylaminomethyl)-2-(2-methylphenyl)-

benzoyl]methionine, lithium salt,
N-[4-N-benzoyl-N-2-cyclohexylethylaminomethyl-2-(2-methylphenyl)benzoyl]-methionine, lithium salt,
N-[4-N-t-butyloxycarbonyl-N-2-cyclohexylethylaminomethyl-2-(2-methyl-phenyl)benzoyl]methionine, lithium salt,
pivaloyloxymethyl N-[4-N-(3-cyclohexyl-1-ethylthiopropan-2-yl)-N-methyl-aminomethyl-2-(2-methylphenyl)benzoyl]methionine, hydrochloride salt,
N-[4-N-(3-cyclohexyl-1-ethylthiopropan-2-yl)-N-methylaminomethyl-2-(2-methylphenyl)benzoyl]-N-methylmethionine, lithium salt,
N-[4-N-(3-cyclohexyl-1-cyclohexylthiopropan-2-yl)-N-methylamino-methyl-2-(2-methylphenyl)benzoyl]methionine, lithium salt,
N-[4-N-(3-cyclohexyl-1-(2-methylphenyl)thiopropan-2-yl)-N-methyl-aminomethyl-2-(2-methylphenyl)benzoyl]methionine, lithium salt,
N-[4-N-(N-phenyl-N-benzenesulfonylaminomethyl)-2-(2-methylphenyl)-benzoyl]methionine, lithium salt,
N-[4-N-(N-phenyl-N-toluenesulfonylaminomethyl)-2-(2-methylphenyl)-benzoyl]methionine, lithium salt,
N-[4-N-(N-phenyl-N-(3-methoxybenzyl)aminomethyl)-2-(2-methylphenyl)-benzoyl]methionine, lithium salt,
N-[4-N-(N-phenyl-N-(4-trifluoromethylbenzenesulfonyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine, lithium salt,
N-[4-N-(N-phenyl-N-(4-chlorobenzyl)aminomethyl)-2-(2-methylphenyl)-benzoyl]methionine, lithium salt,
N-[4-N-(N-phenyl-N-(4-trifluoromethylbenzyl)aminomethyl)-2-(2-methylphenyl)-benzoyl]methionine, lithium salt,
N-[4-N(t-butylcarbazatocarbonylmethyl)amino-2-phenylbenzoyl]methionine,
N-[4-(1-ethoxycarbonylpiperidin-4-ylaminomethyl)-2-(2-methylphenyl-benzoyl]methionine, lithium salt,
N-[4-(N-[3-methylthio-1-carboxyprop-2-yl]aminocarbonyl)-2-phenylbenzoyl]-methionine,
N-[4-N-(furan-2-ylmethyl)-N-isopropylaminomethyl-2-(2-methylphenyl)-benzoyl]methionine, lithium salt,
N-[4-N-(furan-3-ylmethyl)-N-isopropylaminomethyl-2-(2-methylphenyl)-benzoyl]methionine, lithium salt,
N-[4-N-benzyl-N-3-methoxyphenylaminomethyl-2-(2-methylphenyl)-benzoyl]methionine, lithium salt,
N-[4-N-(2-phenylethyl)-N-isopropylaminomethyl-2-(2-methylphenyl)-

benzoyl]methionine, lithium salt,
N-[4-N-benzyl-N-pyrimidin-5-ylaminomethyl-2-(2-methylphenyl)benzoyl]-methionine, lithium salt,
N-[4-N-(1,3-benzodiox-5-yl)-N-pyrimidin-5-ylaminomethyl-2-(2-methyl-phenyl)benzoyl]methionine, lithium salt,
N-[4-N-(1,3-benzodiox-5-yl)-N-pyridizin-2-ylaminomethyl-2-(2-methylphenyl)-benzoyl]methionine, lithium salt,
N-[4-(N-benzyl-N-(2-methoxyphenyl)aminomethyl)-2-(2-methylphenyl)-benzoyl]methionine, lithium salt,
N-[4-(N-benzyl-N-(4-methoxyphenyl)aminomethyl)-2-(2-methylphenyl)-benzoyl]methionine, lithium salt,
N-[4-(N-benzyl-N-(4-acetylphenyl)aminomethyl)-2-(2-methylphenyl)benzoyl]-methionine, lithium salt,
N-[4-(N-benzyl-N-(3-nitrophenyl)aminomethyl)-2-(2-methylphenyl)benzoyl]-methionine, lithium salt,
N-[4-(N-benzyl-N-(4-nitrophenyl)aminomethyl)-2-(2-methylphenyl)-benzoyl]-methionine, lithium salt,
N-[4-N-(N-benzyl-N-(2-acetylphenyl)aminomethyl)-2-(2-methylphenyl)-benzoyl]methionine, lithium salt,
N-[4-N-(N-benzyl-N-(3-acetylphenyl)aminomethyl)-2-(2-methylphenyl)-benzoyl]methionine, lithium salt,
N-[4-N-(N-benzyl-N-(2-chlorophenyl)aminomethyl)-2-(2-methylphenyl)-benzoyl]methionine, lithium salt,
N-[4-N-(N-benzyl-N-(3-chlorophenyl)aminomethyl)-2-(2-methylphenyl)-benzoyl]methionine, lithium salt,
N-[4-N-(N-benzyl-N-(4-chlorophenyl)aminomethyl)-2-(2-methylphenyl)-benzoyl]methionine, lithium salt,
N-[4-(N-benzyl-N-(2-nitrophenyl)aminomethyl)-2-(2-methylphenyl)benzoyl]-methionine, lithium salt,
N-[4-(N-benzyl-N-(2-methylthiophenyl)aminomethyl)-2-(2-methylphenyl)-benzoyl]methionine, lithium salt,
N-[4-(N-benzyl-N-(3-methylthiophenyl)aminomethyl)-2-(2-methylphenyl)-benzoyl]methionine, lithium salt,
N-[4-(N-benzyl-N-(4-methylthiophenyl)aminomethyl)-2-(2-methylphenyl)-benzoyl]methionine, lithium salt,
N-[4-(N-benzyl-N-(4-trifluoromethylphenyl)aminomethyl)-2-(2-methylphenyl)-benzoyl]methionine, lithium salt,

N-[4-N-(4-piperidin-1-ylphenyl)aminomethyl-2-(2-methylphenyl)benzoyl]-methionine,
N-[4-N-(4-morpholin-1-ylphenyl)aminomethyl-2-(2-methylphenyl)benzoyl]-methionine,
N-[4-N-(4-phenoxyphenyl)aminomethyl-2-(2-methylphenyl)benzoyl]-methionine,
N-[4-N-(benzyl-N-thiazol-2-ylmethyl)aminomethyl-2-(2-methylphenyl)-benzoyl]methionine,
N-[4-N-(toluenesulfonyl-N-thiazol-2-ylmethyl)aminomethyl-2-(2-methyl-phenyl)benzoyl]methionine,
N-[4-N-(methanesulfonyl-N-thiazol-2-ylmethyl)aminomethyl-2-(2-methyl-phenyl)benzoyl]methionine,
N-[4-(N-2-cyclohexylethyl-N-cyclopropylaminomethyl)-2-(2-methylphenyl)-benzoyl]methionine,
N-[4-(N-tetrahydrothiopyran-4-yl-N-thiazol-5-ylaminomethyl)-2-(2-methyl-phenyl)benzoyl]methionine,
N-[4-N-t-butyloxycarbonyl-N-(1,3-dicyclohexylpropan-2-yl)aminomethyl-2-(2-methylphenyl)benzoyl]methionine, lithium salt,
N-[4-N-(3-cyclohexyl-1-oxo-1-piperidin-1-ylpropan-2-yl)aminomethyl-2-(2-methylphenyl)benzoyl]methionine, lithium salt,
N-[4-(N-(1-ethylthio-4-methylpentan-2-yl)aminomethyl)-2-(2-methylphenyl)-benzoyl]methionine,
N-[4-(N-(1-ethylthio-4-methylpentan-2-yl)-N-methylaminomethyl)-2-(2-methylphenyl)benzoyl]methionine,
N-[4-(N-(1,3-dicyclohexylpropan-2-yl)-N-methylaminomethyl)-2-(2-methyl-phenyl)benzoyl]methionine,
N-[4-(N-(1,3-dicyclohexylpropan-2-yl)-N-methylaminomethyl)-2-(2-methyl-phenyl)benzoyl]methionine,
N-[4-(N-acetyl-N-(1,3-dicyclohexylpropan-2-yl)aminomethyl)-2-(2-methyl-phenyl)benzoyl]methionine,
N-[4-(N-benzoyl-N-(1,3-dicyclohexylpropan-2-yl)aminomethyl)-2-(2-methyl-phenyl)benzoyl]methionine,
N-[4-(N-benzenesulfoyl-N-(1,3-dicyclohexylpropan-2-yl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine,
N-[4-(N-(N,N-dibutylacetamido)aminomethyl)-2-(2-methylphenyl)benzoyl]-methionine,
N-[4-(N-(N,N-dibutylacetamido)-N-methylaminomethyl)-2-(2-methylphenyl)-

benzoyl]methionine,
N-[4-(N-(N,N-dibenzylacetamido)aminomethyl)-2-(2-methylphenyl)benzoyl]-methionine,
N-[4-(N-(2-cyclohexylethyl)-N-isopropylaminomethyl)-2-(2-methylphenyl)-benzoyl]methionine,
N-[4-(N-butanesulfonyl-N-(2-cyclohexylethyl)aminomethyl)-2-(2-methyl-phenyl)benzoyl]methionine,
N-[4-(N,N-dibutylaminomethyl)-2-(2-methylphenyl)benzoyl]methionine,
N-[4-(N-butanesulfonyl-N-(3-phenylpropyl)aminomethyl)-2-(2-methylphenyl)-benzoyl]methionine,
N-[4-(N-butyl-N-(2-phenylethyl)aminomethyl)-2-(2-methylphenyl)benzoyl]-methionine,
N-[4-N-(3-cyclohexyl-1-ethylthiopropan-2-yl)-N-methylaminomethyl-2-(2-methylphenyl)benzoyl]methionine, hydrochloride,
N-[4-N-(3-cyclohexyl-1-ethylthiopropan-2-yl)-N-isobutylaminomethyl-2-(2-methylphenyl)benzoyl]methionine,
N-[4-N-(3-cyclohexyl-1-ethylthiopropan-2-yl)-N-formylaminomethyl-2-(2-methylphenyl)benzoyl]methionine,
N-[4-N-acetyl-N-(3-cyclohexyl-1-ethylthiopropan-2-yl)aminomethyl-2-(2-methylphenyl)benzoyl]methionine,
N-[4-N-t-butyloxycarbonyl-N-(3-cyclohexyl-1-ethylthiopropan-2-yl)amino-methyl-2-(2-methylphenyl)benzoyl]methionine,
N-[4-N-benzoyl-N-(3-cyclohexyl-1-ethylthiopropan-2-yl)aminomethyl-2-(2-methylphenyl)-benzoyl]methionine,
N-[4-N-butanesulfoyl-N-(3-cyclohexyl-1-ethylthiopropan-2-yl)amino-methyl-2-(2-methylphenyl)benzoyl]methionine,
N-[4-N-benzenesulfonyl-N-(3-cyclohexyl-1-ethylthiopropan-2-yl)amino-methyl-2-(2-methylphenyl)benzoyl]methionine,
N-[4-(N-5-(4-chlorophenyl)furan-2-ylmethyl-N-isopropylaminomethyl)-2-(2-methylphenyl)benzoyl]methionine, lithium salt,
N-[4-(N-methyl-N-(1,1-dimethyl-2-phenylethyl)aminomethyl)-2-(2-methyl-phenyl)benzoyl]methionine, lithium salt,
N-[4-(N-methyl-N-(1,1-dimethyl-2-cyclohexylethyl)aminomethyl)-2-(2-methylphenyl)-benzoyl]methionine, lithium salt,
N-[4-(N-2-cyclohexylethyl-N-thiazol-5-ylmethylaminomethyl)-2-(2-methyl-phenyl)benzoyl]methionine,
N-[4-(1-ethylthio-4-phenylbut-2-oxymethyl)-2-(2-methylphenyl)-benzoyl]-

methionine,
N-[4-N-benzyl-N-(4-cyanophenyl)aminomethyl-2-(2-methylphenyl)benzoyl]-methionine, lithium salt,
N-[4-N-benzyl-N-(4-carboxamidophenyl)aminomethyl-2-(2-methylphenyl)-benzoyl]methionine, lithium salt,
N-[4-N-benzyl-N-(4-sulfonamidophenyl)aminomethyl-2-(2-methylphenyl)-benzoyl]methionine, lithium salt,
N-[4-N-benzyl-N-(4-N-benzoylsulfonamidophenyl)aminomethyl-2-(2-methyl-phenyl)benzoyl]methionine, lithium salt,
N-[4-N-benzyl-N-(4-propionylphenyl)aminomethyl-2-(2-methylphenyl)-benzoyl]methionine, lithium salt,
N-[4-N-benzyl-N-(4-benzoylphenyl)aminomethyl-2-(2-methylphenyl)-benzoyl]methionine, lithium salt,
N-[4-N-benzyl-N-(4-(6-methylbenzthiazol-2yl)phenyl)aminomethyl-2-(2-methylphenyl)benzoyl]methionine, lithium salt,
N-[4-N-2,5-difluorobenzyl-N-(4-cyanophenyl)aminomethyl-2-(2-methyl-phenyl)benzoyl]methionine, lithium salt,
N-[4-N-2,4-difluorobenzyl-N-(4-cyanophenyl)aminomethyl-2-(2-methyl-phenyl)benzoyl]methionine, lithium salt,
N-[4-N-3,5-difluorobenzyl-N-(4-cyanophenyl)aminomethyl-2-(2-methyl-phenyl)benzoyl]methionine, lithium salt,
N-[4-N-3,5-difluorobenzyl-N-(4-vinylphenyl)aminomethyl-2-(2-methyl-phenyl)benzoyl]methionine, lithium salt,
N-[4-N-3,5-difluorobenzyl-N-(4-acetylphenyl)aminomethyl-2-(2-methyl-phenyl)benzoyl]methionine, lithium salt,
N-[4-N-3,5-difluorobenzyl-N-(4-(1-hydroxyethyl)phenyl)aminomethyl-2-(2-methylphenyl)benzoyl]methionine, lithium salt,
N-[4-N-3,5-difluorobenzyl-N-(4-(1-hydroxy-1-phenylmethyl)phenyl)-aminomethyl-2-(2-methylphenyl)benzoyl]methionine, lithium salt,
N-[4-N-3,5-difluorobenzyl-N-(4-(2-hydroxyethyl)phenyl)aminomethyl-2-(2-methylphenyl)benzoyl]methionine, lithium salt,
N-[4-N-3,5-difluorobenzyl-N-(4-(2-tert-butyldimethylsiloxyethyl)phenyl)-aminomethyl-2-(2-methylphenyl)benzoyl]methionine, lithium salt,
N-[4-N-3,5-difluorobenzyl-N-(1-ethylthio-3-cyclohexylprop-2-yl)amino-methyl-2-(2-methylphenyl)benzoyl]methionine,
N-[4-(2-N-piperidin-1-ylaminoethenyl)-2-(2-methylphenyl)benzoyl]methionine, lithium salt,

N-[4-(2-N-2-methoxymethylpyrrolidin-1-ylaminoethenyl)-2-(2-methylphenyl)-benzoyl]methionine, lithium salt,
N-[4-N-(4-trans-pentafluorophenoxycyclohexyl)aminomethyl-2-(2-methyl-phenyl)benzoyl]methionine,
N-[4-(N-(2-cyclohexylethyl)-N-methylaminomethyl)-2-(2-methylphenyl)-benzoyl]glutamine, trifluoroacetic acid salt,
N-[4-(N-(2-cyclohexylethyl)-N-methylaminomethyl)-2-(2-methylphenyl)-benzoyl]homocysteine, lithium salt,
N-[4-(N-(2-cyclohexylethyl)-N-methylaminomethyl)-2-(2-methylphenyl)-benzoyl]histidine, trifluoroacetic acid salt,
N-[4-(N-cyclohexylmethylaminoethyl)-2-(2-methylphenyl)benzoyl]methionine, lithium salt,
N-[4-(N,N-di-(cyclohexylmethyl)aminoethyl)-2-(2-methylphenyl)benzoyl]-methionine, lithium salt,
N-[4-(N-cyclohexylmethyl-N-phenylacetylaminoethyl)-2-(2-methylphenyl)-benzoyl]methionine, lithium salt,
N-[4-(N-cyclohexylmethyl-N-1-adamantanoylaminoethyl)-2-(2-methylphenyl)-benzoyl]methionine, lithium salt,
N-[4-(N-cyclohexylmethyl-N-t-butoxycarbonylaminoethyl)-2-(2-methylphenyl)-benzoyl]methionine, lithium salt,
N-[4-(N-cyclohexylmethyl-N-2-ethylhexyloxycarbonylaminoethyl)-2-(2-methyl-phenyl)benzoyl]methionine, lithium salt,
N-[4-(N-cyclohexylmethyl-N-2,2,2-trichloroethoxycarbonylaminoethyl)-2-(2-methylphenyl)benzoyl]methionine, lithium salt,
N-[4-(N-cyclohexylmethyl-N-cyclohexyloxycarbonylaminoethyl)-2-(2-methyl-phenyl)benzoyl]methionine, lithium salt,
N-[4-(N-cyclohexylmethyl-N-adamantyloxycarbonylaminoethyl)-2-(2-methyl-phenyl)benzoyl]methionine, lithium salt,
N-[4-(N-cyclohexylmethyl-N-phenoxycarbonylaminoethyl)-2-(2-methylphenyl)-benzoyl]methionine, lithium salt,
N-[4-(N-cyclohexylmethyl-N-benzyloxycarbonylaminoethyl)-2-(2-methyl-phenyl)benzoyl]methionine, lithium salt,
N-[4-(N-cyclohexylmethyl-N-adamant-1-aminocarbonylaminoethyl)-2-(2-methylphenyl)benzoyl]methionine, lithium salt,
N-[4-(N-cyclohexylmethyl-N-adamant-1-aminothiocarbonylaminoethyl)-2-(2-methylphenyl)benzoyl]methionine, lithium salt,
N-[4-(N-(2-cyclohexylethyl)-N-methylaminomethyl)-2-(2-methylphenyl)-

benzoyl]glutaminitrile, lithium salt,
N-[4-(N-p-toluenesulfonyl-N-methylaminomethyl)-2-(2-methylphenyl)-benzoyl]methionine, lithium salt,
N-[4-(N-(4-benzyloxybenzyl)-N-(N-2-methyl-2-phenylpropylacetamido)-aminomethyl)-2-(2-methylphenyl)benzoyl]methionine, lithium salt,
N-[4-(N-(2-cyclohexenylethyl)-N-methylaminomethyl)-2-(2-methylphenyl)-benzoyl]methionine, lithium salt,
(2S) 2-N-[4-(N-(2-cyclohexylethyl)-N-methylaminomethyl)-2-(2-methyl-phenyl)benzoyl]amino-4-methylsulfenylbutanoate, lithium salt,
(2S) 2-N-[4-(N-(2-cyclohexylethyl)-N-methylaminomethyl)-2-(2-methylphenyl)benzoyl]amino-4-methylsulfonylbutanoate, lithium salt,
N-[4-(N-(2-cyclohexylethyl)-N-methylaminomethyl)-2-(2-methylphenyl)-benzoyl]norleucine, lithium salt,
N-[4-(N-(2-cyclohexylethyl)-N,N-dimethylaminomethyl)-2-(2-methylphenyl)-benzoyl]methionine,
(2S) 2-N-[4-(N-(2-cyclohexylethyl)-N-butylaminomethyl)-2-(2-methylphenyl)-benzoyl]amino-4-methylsulfenylbutanoate, lithium salt,
N-[4-(N-(2-cyclohexylethyl)-N-p-toluenesulfonylaminomethyl)-2-(2-methyl-phenyl)benzoyl]methionine, lithium salt,
N-[4-(N-(2-cyclohexylethyl)-N-m-toluenesulfonylaminomethyl)-2-(2-methyl-phenyl)benzoyl]methionine, lithium salt,
N-[4-(N-(2-cyclohexylethyl)-N-p-tert-butylbenzenesulfonylaminomethyl)-2-(2-methylphenyl)benzoyl]methionine, lithium salt,
N-[4-(N-(2-cyclohexylethyl)-N-p-bromobenzenesulfonylaminomethyl)-2-(2-methylphenyl)benzoyl]methionine, lithium salt,
N-[4-(N-(2-cyclohexylethyl)-N-p-methoxybenzenesulfonylaminomethyl)-2-(2-methylphenyl)benzoyl]methionine, lithium salt,
N-[4-(N-(2-cyclohexylethyl)-N-p-nitrobenzenesulfonylaminomethyl)-2-(2-methylphenyl)benzoyl]methionine, lithium salt,
N-[4-(N-(2-cyclohexyl-2-methylpropyl)-N-methylaminomethyl)-2-(2-methyl-phenyl)benzoyl]methionine, lithium salt,
N-[4-(3-cyclohexyl-1-methoxyprop-2-ylaminomethyl)-2-(2-methylphenyl)-benzoyl]methionine, lithium salt,
N-[4-(1-ethylsulfenyl-3-cyclohexylprop-2-ylaminomethyl)-2-(2-methylphenyl)-benzoyl]methionine, lithium salt,
(2S)-2-N-[4-(1-ethylsulfenyl-3-cyclohexylprop-2-ylaminomethyl)-2-(2-methyl-phenyl)benzoyl]amino-4-methylsulfenylbutanoate, lithium salt,

N-[4-(N-(3-cyclohexylpropyl)-N-benzenesulfonylaminomethyl)-2-(2-methylphenyl)benzoyl]methionine, lithium salt,
N-[4-(N-glucosaminomethyl)-2-(2-methylphenyl)benzoyl]methionine, lithium salt,
(2S)-2-N-[4-(N-2-cyclohexylethyl-N-methylaminomethyl)-2-(2-methylphenyl)-benzoyl]amino-4-difluoromethylthiobutanoate, lithium salt,
(2S)-2-N-[4-(N-2-cyclohexylethyl-N-methylaminomethyl)-2-(2-methylphenyl)-benzoyl]amino-5-methoxypentanoate, lithium salt,
(2S)-2-N-[4-(N-2-cyclohexylethyl-N-methylaminomethyl)-2-(2-methylphenyl)-benzoyl]aminopent-4-ynoate, lithium salt,
2-[4-(N-2-cyclohexylethyl-N-methylaminomethyl)-2-(2-methylphenyl)-benzoyl]oxy-4-methylthiobutanoate, lithium salt,
N-[4-(N-(5-bromo-(4-chlorophenyl)furan-2-ylmethyl-N-isopropyl-amino-methyl)-2-(2-methylphenyl)benzoyl]methionine, lithium salt,
N-[4-(N-(5-phenyl-(4-chlorophenyl)furan-2-ylmethyl-N-isopropyl-aminomethyl)-2-(2-methylphenyl)benzoyl]methionine, lithium salt,
N-[4-(N-(5-(3-methoxyphenyl)-(4-chlorophenyl)furan-2-ylmethyl)-N-isopropylaminomethyl)-2-(2-methylphenyl)benzoyl]methionine, lithium salt,
N-[4-(N-(4,5-di(4-chlorophenyl)furan-2-yl)methyl)-N-isopropylamino-methyl)-2-(2-methylphenyl)benzoyl]methionine, lithium salt,
N-[4-(N-(5-thien-3-yl-(4-chlorophenyl)furan-2-yl)methyl)-N-isopropyl-aminomethyl)-2-(2-methylphenyl)benzoyl]methionine, lithium salt,
N-[4-(N-(2-cyclohexylethyl)-N-2-fluoroethylaminomethyl)-2-(2-methylphenyl)benzoyl]methionine,
N-[4-(N-(2-cyclohexylethyl)-N-2,2,2-trifluoroethylaminomethyl)-2-(2-methylphenyl)benzoyl]methionine, lithium salt,
N-[4-(N-(2-cyclohexylethyl)-N-2-methoxyethylaminomethyl)-2-(2-methylphenyl)benzoyl]methionine,
N-[4-(N-(2-cyclohexylethyl)-N-2-methylthioethylaminomethyl)-2-(2-methylphenyl)benzoyl]methionine,
N-[4-(N-(2-cyclohexylethyl)-N-1-methyl-2(S)-methylthioethylaminomethyl)-2-(2-methylphenyl)benzoyl]methionine,
N-[4-(N-(2-cyclohexylethyl)-N-2-N,N-dimethylaminomethyl)-2-(2-methylphenyl)benzoyl]methionine,
N-[4-(N-(1-benzyloxymethyl-2-(S)-ethylthioethylaminomethyl)-2-(2-methylphenyl)benzoyl]methionine,
N-[4-(N-(2-cyclohexylethyl)-N-methylaminomethyl)-2-(2-methylphenyl)-

benzoyl]ornithine, trifluoroacetate salt,
N-[4-(N-(2-cyclohexylethyl)-N-2-N-methylaminomethyl)-2-(2-methylphenyl)-benzoyl]thien-2-ylalanine,
N-[4-(1-ethylthio-3-cyclohexylprop-2-ylaminomethyl)-5-fluoro-2-(2-methyl-phenyl)benzoyl]methionine,
N-[4-(N-butyl-N-4-cyclohexylbenzylaminomethyl)-2-(2-methylphenyl)benzoyl]-methionine, lithium salt,
N-[4-(N-butyl-N-4-cyclohexylbenzoylaminomethyl)-2-(2-methylphenyl)-benzoyl]methionine, lithium salt,
N-[4-(N-cyclohexylaminocarbonylethyl)-2-(2-methylphenyl)benzoyl]-methionine, lithium salt,
N-[4-(N-cyclohexylmethyl-N-butylaminoethyl)-2-(2-methylphenyl)benzoyl]-methionine, lithium salt,
N-[4-(N-cyclohexylmethyl-N-butylaminocarbonylmethyl)-2-(2-methylphenyl)-benzoyl]methionine, lithium salt,
N-[4-(N-cyclohexanoyl-N-butylaminoethyl)-2-(2-methylphenyl)benzoyl]-methionine, lithium salt,
N-[4-(N-cyclohexylmethyl-N-butanoylaminoethyl)-2-(2-methylphenyl)benzoyl]-methionine lithium salt,
N-[4-(N-cyclohexylpropyl)-2-(2-methylphenyl)benzoyl]methionine, lithium salt,
N-[4-(N-cyclohexyl-N-propanoylaminopropyl)-2-(2-methylphenyl)benzoyl]-methionine,
N-[4-(N-cyclohexyl-N-butylaminopropyl)-2-(2-methylphenyl)benzoyl]-methionine, lithium salt,
N-[4-(N-cyclohexyl-N-methylaminocarbonylethyl)-2-(2-methylphenyl)benzoyl]-methionine, lithium salt,
N-[4-(N-cyclohexyl-N-butylaminocarbonylethyl)-2-(2-methylphenyl)benzoyl]-methionine, lithium salt,
N-[4-(N,N-dicyclohexylaminocarbonylethyl)-2-(2-methylphenyl)benzoyl]-methionine, lithium salt,
N-[4-(N-adamant-1-ylaminocarbonylethyl)-2-(2-methylphenyl)benzoyl]-methionine, lithium salt,
N-[4-(N-adamant-2-ylaminocarbonylethyl)-2-(2-methylphenyl)benzoyl]-methionine, lithium salt,
N-[4-(N-adamant-1-ylmethylaminocarbonylethyl)-2-(2-methylphenyl)benzoyl]-methionine, lithium salt,
N-[4-(N-mytanylmethylaminocarbonylethyl)-2-(2-methylphenyl)benzoyl]-

methionine, lithium salt,
N-[4-(N-cyclooctanylaminocarbonylethyl)-2-(2-methylphenyl)-benzoyl]-methionine, lithium salt,
3-[4-(N-cyclohexyl-N-methylaminomethyl)-2-(2-methylphenyl)benzoylmethyl]-4-methylthiobutyric acid,
N-[4-(N-butylaminocarbonylmethyl)-2-(2-methylphenyl)benzoyl]methionine, lithium salt,
N-[4-(N-(2,2,4,4-tetramethylbutylamino)carbonylethyl)-2-(2-methylphenyl)-benzoyl]methionine, lithium salt,
N-[4-(N,N-dibutylaminopropyl)-2-(2-methylphenyl)benzoyl]methionine, lithium salt,
N-[4-N-(2-ethylphenyl)aminomethyl-2-(2-methylphenyl)benzoyl]methionine,
N-[4-N-(2-propylphenyl)aminomethyl-2-(2-methylphenyl)benzoyl]methionine,
N-[4-N-(2-butylphenyl)aminomethyl-2-(2-methylphenyl)benzoyl]methionine,
N-[4-N-(4-butylphenyl)aminomethyl-2-(2-methylphenyl)benzoyl]methionine,
N-[4-N-(2-butylphenyl)-N-(3,5-difluorobenzyl)aminomethyl-2-(2-methyl-phenyl)benzoyl]methionine,
N-[4-N-(2,6-diethylphenyl)-N-(3,5-difluorobenzyl)aminomethyl-2-(2-methyl-phenyl)benzoyl]methionine, lithium salt,
N-[4-N-(2-butylphenyl)-N-(cyclohexylmethyl)aminomethyl-2-(2-methylphenyl)-benzoyl]methionine, lithium salt,
N-[4-N-(2-cyclohexylethyl)-N-(3-methylphenyl)aminomethyl-2-(2-methyl-phenyl)benzoyl]methionine,
N-[4-N-(2-butylphenyl)-N-(2-cyclohexylethyl)aminomethyl-2-(2-methyl-phenyl)benzoyl]methionine,
N-[4-N-butyl-N-(2-(3,5-difluoro)phenylethyl)aminomethyl-2-(2-methylphenyl)-benzoyl]methionine,
N-[4-N-butanesulfonyl-N-(2-phenylethyl)aminomethyl-2-(2-methylphenyl)-benzoyl]methionine lithium salt,
N-[4-N-(2-cyclohexylethyl)-N-methylaminomethyl-2-(2-methylphenyl)-benzoyl]-3-aminotetrahydrofuran-2-one,
N-[4-(N-(-2-cyclohexylethyl)-N-butylaminomethyl)-2-(2-methylphenyl)-benzoyl]methionine, lithium salt,
N-[4-N-butyl-N-(2-cyclohexylethyl)aminomethyl-2-(2-methylphenyl)benzoyl]-methionine 4-methylphenylsulfonimide,
N-[4-N-butyl-N-(1-phenyltetrazol-5-yl)aminomethyl-2-(2-methylphenyl)-benzoyl]methionine,

N-[4-N-t-butyl-N-(2-cyclohexylethyl)aminomethyl-2-(2-methylphenyl)-benzoyl]methionine,
N-[4-N-(2-cyclohexylethyl)-N-(pent-2-yl)aminomethyl-2-(2-methylphenyl)-benzoyl]methionine,
N-[4-N-(2-cyclohexylethyl)-N-(pent-2-yl)aminomethyl-2-(2-methylphenyl)-benzoyl]methionine,
N-[4-N-(2-cyclohexylethyl)-N-propyloxyaminomethyl-2-(2-methylphenyl)-benzoyl]methionine, lithium salt,
N-[4-N-(2-cyclohexylethyl)-N-propanesulfonylaminomethyl-2-(2-methyl-phenyl)benzoyl]methionine,
N-[4-N-(3-chloropropanesulfonyl)-N-(2-cyclohexylethyl)aminomethyl-2-(2-methylphenyl)benzoyl]methionine,
N-[4-N-(2-cyclohexylethyl)-N-(3-ethoxypropanesulfonyl)aminomethyl-2-(2-methylphenyl)benzoyl]methionine lithium salt,
N-[4-N-(2-cyclohexylethyl)-N-(3-trifluoromethylpropanesulfonyl)amino-methyl-2-(2-methylphenyl)benzoyl]methionine,
N-[4-N-(butanesulfonyl)-N-(3-cyclohexylpropyl)aminomethyl-2-(2-methyl-phenyl)benzoyl]methionine, lithium salt,
N-[4-N-(4-cyclohexyl-1-ethylthiobutan-2-yl)aminomethyl-2-(2-methylphenyl)-benzoyl]methionine,
N-[4-N-(butanesulfonyl)-N-(4-cyclohexylbutyl)aminomethyl-2-(2-methyl-phenyl)benzoyl]methionine, lithium salt,
N-[4-N-butyl-N-quinolin-2-ylaminomethyl-2-(2-methylphenyl)benzoyl]-methionine,
N-[4-(N-butyl-N-(2-piperidin-1-ylethyl)aminomethyl)-2-(2-methylphenyl)-benzoyl]methionine,
N-[4-N-((1-norpholinocarbonyl)butyl)aminomethyl-2-(2-methylphenyl)-benzoyl]methionine,
N-[4-N-butyl-N-(2-morpholin-4-ylethyl)aminomethyl-2-(2-methylphenyl)-benzoyl]methionine,
N-[4-N-butyl-N-(fluoren-9-yl)aminomethyl-2-(2-methylphenyl)benzoyl]-methionine,
N-[4-N-(2-cyclohexylethyl)-N-(furan-2-ylmethyl)aminomethyl-2-(2-methyl-henyl)benzoyl]methionine,
N-[4-N-butyl-N-(2-pyrrolidin-1-ylethyl)aminomethyl-2-(2-methylphenyl)-benzoyl]methionine,
N-[4-N-(2-butylphenyl)-N-(thiazol-5-ylmethyl)aminomethyl-2-(2-methyl-

phenyl)benzoyl]methionine,
N-[4-N-((2-ethylthio)-1,3,4-thiadiazol-5-yl)aminomethyl-2-(2-methylphenyl)-benzoyl]methionine,
N-[4-N-butyl-N-((2-ethylthio)-1,3,4-thiadiazol-5-yl)aminomethyl-2-(2-methyl-phenyl)benzoyl]methionine,
N-[4-(N-butyl-N-(2-phenylethyl)aminomethyl)-2-(2-methylphenyl)benzoyl]-methionine p-tolylsulfonimide, hydrochloride salt,
N-[4-(N-butyl-N-(2-phenylethyl)aminomethyl)-2-(2-methylphenyl)-benzoyl]methionine 4-(aminomethyl)phenylsulfonimide, dihydrochloride salt,
N-[4-(N-butyl-N-(2-phenylethyl)aminomethyl)-2-(2-methylphenyl)-benzoyl]methionine, isopropylsulfonimide,
N-[4-N-(N-phenyl-N-(4-fluorobenzoyl)aminomethyl)-2-(2-methylphenyl)-benzoyl]methionine, lithium salt,
N-[4-N-(N-phenyl-N-(n-butanesulfonyl)aminomethyl)-2-(2-methylphenyl)-benzoyl]methionine, lithium salt,
N-[4-N-(N-phenyl-N-(3-nitrobenzenesulfonyl)aminomethyl)-2-(2-methyl-phenyl)benzoyl]methionine, lithium salt,
N-[4-N-(N-phenyl-N-(4-fluorobenzenesulfonyl)aminomethyl)-2-(2-methyl-phenyl)benzoyl]methionine, lithium salt,
N-[4-N-(N-phenyl-N-(4-ethylbenzenesulfonyl)aminomethyl)-2-(2-methyl-phenyl)benzoyl]methionine, lithium salt,
N-[4-N-(N-phenyl-N-(4-nitrobenzenesulfonyl)aminomethyl)-2-(2-methyl-phenyl)benzoyl]methionine, lithium salt,
N-[4-N-(N-phenyl-N-(2,3-dichlorobenzenesulfonyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine, lithium salt,
N-[4-N-(N-3,4-(methylenedioxy)phenyl-N-(4-fluorobenzyl)-aminomethyl)-2-(2-methylphenyl)benzoyl]methionine, lithium salt,
N-[4-N-(N-3,4-(methylenedioxy)phenyl-N-(4-fluorobenzyl)-aminomethyl)-2-(2-methylphenyl)benzoyl]methionine, lithium salt,
N-[4-N-(N-phenyl-N-(2-fluorobenzyl)aminomethyl)-2-(2-methylphenyl)-benzoyl]methionine, lithium salt,
N-[4-N-(N-phenyl-N-(3-fluorobenzyl)aminomethyl)-2-(2-methylphenyl)-benzoyl]methionine, lithium salt,
N-[4-N-(N-phenyl-N-(4-fluorobenzyl)aminomethyl)-2-(2-methylphenyl)-benzoyl]methionine, lithium salt,
N-[4-N-(N-phenyl-N-(4-bromobenzyl)aminomethyl)-2-(2-methylphenyl)-benzoyl]methionine, lithium salt,

N-[4-N-(N-phenyl-N-(4-cyanobenzyl)aminomethyl)-2-(2-methylphenyl)-benzoyl]methionine, lithium salt,
N-[4-N-(N-phenyl-N-(4-methoxybenzyl)aminomethyl)-2-(2-methylphenyl)-benzoyl]methionine, lithium salt,
N-[4-N-(N-phenyl-N-(4-trifluoromethoxybenzyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine, lithium salt,
N-[4-N-(N-phenyl-N-(4-nitrobenzyl)aminomethyl)-2-(2-methylphenyl)-benzoyl]methionine, lithium salt,
N-[4-N-(N-phenyl-N-(4-carboxylic acid benzyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine, dilithium salt,
N-[4-N-(N-phenyl-N-(4-phenylbenzyl)aminomethyl)-2-(2-methylphenyl)-benzoyl]methionine, lithium salt,
N-[4-N-(N-phenyl-N-(4-N-carboxymethionine)benzyl)aminomethyl-2-(2-methylphenyl)benzoyl]methionine, dilithium salt,
N-[4-N-(N-phenyl-N-(2-naphthyl)aminomethyl)-2-(2-methylphenyl)-benzoyl]methionine, lithium salt,
N-[4-N-(N-phenyl-N-(9-methyl-anthracene-yl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine, lithium salt,
N-[4-N-(N-phenyl-N-(2-methyl-anthraquinone-yl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine, lithium salt,
N-[4-N-(N-phenyl-N-(2,3-difluorobenzyl)aminomethyl)-2-(2-methylphenyl)-benzoyl]methionine, lithium salt,
N-[4-N-(N-phenyl-N-(2,4-difluorobenzyl)aminomethyl)-2-(2-methylphenyl)-benzoyl]methionine, lithium salt,
N-[4-N-(N-phenyl-N-(2-thiophenesulfonyl)aminomethyl)-2-(2-methylphenyl)-benzoyl]methionine, lithium salt,
N-[4-N-(N-phenyl-N-(2-methyl-4-methylemethiazolyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine, lithium salt,
N-[4-N-(N-3,5-difluorophenyl-N-(5-thiazolylmethyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine, lithium salt,
N-[4-N-(N-(5-thiazolylmethyl)-N-(3,5-difluorobenzyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine, lithium salt,
N-[4-N-(N-phenyl-N-(3,5-difluorobenzyl)aminomethyl)-2-(2-methylphenyl)-benzoyl]methionine, lithium salt,
N-[4-N-(N-(4-acetonitrilephenyl-N-(3,5-difluorobenzyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine, lithium salt,
N-[4-N-(N-phenyl-N-(3-methoxy-5-nitrobenzyl)aminomethyl)-2-(2-

methylphenyl)benzoyl]methionine, lithium salt,
N-[4-N-(N-(4-nitrophenyl-N-(4-methoxybenzyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine, lithium salt,
N-[4-N-(N-butyl-N-(3,5-difluorobenzyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine, lithium salt,
N-[4-N-(N-(4,4,4-trifluorobutyl-N-(3,5-difluorobenzyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine, lithium salt,
N-[4-N-(N-cyclohexyl-N-(3,5-difluorobenzyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine, lithium salt,
N-[4-N-(N-(4-cyclohexanonyl)-N-(3,5-difluorobenzyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine, lithium salt,
N-[4-N-(N-(4-(2,2-dimethyltrimethylene ketal)-cyclohexyl)-N-(3,5-difluorobenzyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine, lithium salt,
N-[4-N-(N-cyclohexylmethyl-N-(2,4-difluorobenzyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine, lithium salt,
N-[4-N-(N-cyclohexylmethyl-N-(3,5-difluorobenzyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine, lithium salt,
N-[4-N-(N-(4-cyanobenzyl)-N-(3,5-difluorobenzyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine, lithium salt,
N-[4-N-(N-(3,5-difluorobenzyl)-N-(4-N-carboxymethionine)benzyl)-aminomethyl-2-(2-methylphenyl)benzoyl]methionine, dilithium salt,
N-[4-N-(N-(2-cyclohexylethyl-N-(3,5-difluorobenzyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine, lithium salt,
N-[4-N-(N-(3-methylthiopropyl)-N-(3,5-difluorobenzyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine, lithium salt,
N-[4-N-(N-cyclopropyl-N-(2-(3,5-difluorophenyl)ethyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine, lithium salt,
[4-N-(N-2-methylbutyl-N-(2-(2,4-difluorophenyl)ethyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine, lithium salt,
[4-N-(N-butyl-N-(2-(2,4-difluorophenyl)ethyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine, lithium salt,
N-[4-N-(N-(4-methyltetrahydropyran-yl)-N-(3,5-difluorobenzyl)-aminomethyl)-2-(2-methylphenyl)benzoyl]methionine, lithium salt,
N-[4-N-(N-(4-methyltetrahydrothiopyran-yl)-N-(3,5-difluorobenzyl)-aminomethyl)-2-(2-methylphenyl)benzoyl]methionine, lithium salt,
N-[4-N-(N-(4-tetrahydropyran-yl)-N-(3,5-difluorobenzyl)aminomethyl)-2-(2-

methylphenyl)benzoyl]methionine, lithium salt,
N-[4-(N-(3-cyclohexyl-1-ethylthioprop-2-yl)aminomethyl)-2-(2-methylphenyl)benzoyl]amino-4-methylsulfonylbutanoate, lithium salt,
N-[4-(N-methyl-N-(2-cyclohexylethyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine, p-tolylsulfonimide,
N-[4-N-(N-(trans-4-hydroxycyclohexyl)-N-(3,5-difluorobenzyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine, lithium salt,
N-[4-N-(N-(cis-4-hydroxycyclohexyl)-N-(3,5-difluorobenzyl)-aminomethyl)-2-(2-methylphenyl)benzoyl]methionine, lithium salt,
(2S) 2-N-[4-(1-ethylthio-3-cyclohexylprop-2-ylaminomethyl)-2-(2-methylphenyl)benzoyl]amino-4-methylsulfenylbutanoate, lithium salt,
N-[4-(N-(2-(1,3-dioxan-2-ylethyl)-N-butylaminomethyl)-2-(2-methylphenyl)-benzoyl]methionine,
N-[4-(N-(2-cyclohexylethyl)-N-methylaminomethyl)-2-(2-methylphenyl)-benzoyl]thioglutamine, lithium salt,
N-[4-(1-ethylthio-3-cyclohexylprop-2-ylaminomethyl)-5-methoxy-2-(2-methylphenyl)benzoyl]methionine,
N-[4-(1-ethylthio-3-cyclohexylprop-2-ylaminomethyl)-5-N'N'-dimethyl-amino-2-(2-methylphenyl)benzoyl]methionine,
N-[4-N-(6-fluorobenzothiazol-2-yl)aminomethyl-2-(2-methylphenyl)-benzoyl]methionine, and
N-[4-N-butyl-N-(furan-2-ylmethyl)aminomethyl-2-(2-methylphenyl)benzoyl]-methionine.

11. A compound according to claim 10 selected from the group consisting of
[4-(1-ethylthio-3-cyclohexylprop-2-ylaminomethyl)-2-(2-methylphenyl)-benzoyl]methionine,
N-[4-(N-(2-cyclohexylethyl)-N-methylaminomethyl)-2-(2-methylphenyl)-benzoyl]methionine, lithium salt, and
N-[4-(N-(-2-cyclohexylethyl)-N-butylaminomethyl)-2-(2-methylphenyl)-benzoyl]methionine, lithium salt.

12. A method of inhibiting protein isoprenyl transferases in a mammal in need of such treatment comprising administering to the mammal a therapeutically effective amount of a compound of claim 1.

13. A composition for inhibiting protein isoprenyl transferases comprising a

pharmaceutical carrier and a therapeutically effective amount of a compound of claim 1.

14. A method for inhibiting or treating cancer in a mammal, comprising administering to the mammal a therapeutically effective amount of a compound of claim 1 alone or in combination with another chemotherapeutic agent.

15. A composition for the treatment of cancer comprising a compound of claim 1 in combination with another chemotherapeutic agent and a pharmaceutically acceptable carrier.

16. A method for inhibiting post-translational modification of the oncogenic Ras protein by protein farnesyltransferase, protein geranylgeranyltransferase, or both in a mammal comprising administering to the mammal a therapeutically effective amount of a compound of claim 1.

17. A composition for inhibiting post-translational modification of the oncogenic Ras protein by protein farnesyltransferase, protein geranylgeranyltransferase, or both comprising a compound of claim 1 in combination with a pharmaceutical carrier.

18. A method for treating or preventing intimal hyperplasia associated with restenosis and atherosclerosis in a mammal comprising administering to the mammal a therapeutically effective amount of a compound of claim 1.

19. A composition for treating or preventing restenosis in a mammal comprising a compound of claim 1 in combination with a pharmaceutically acceptable carrier.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US98/09296

A. CLASSIFICATION OF SUBJECT MATTER

IPC(6) :Please See Extra Sheet.
US CL :Please See Extra Sheet.

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : Please See Extra Sheet.

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

CAS ONLINE

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	Database HCAPLUS on STN, 1997:247953, BOYLE, F.T. et al. 'Preparation of 2-aminomethyl-4-mercaptopyrrolidines and analogs as farnesyl trasferase inhibitors', 20 February 1997, PCT Int. Appl. 189 pp., see the entire abstract.	1-19
X	Database HCAPLUS on STN. 1996:567259 SEBTI et al. 'Peptidomimetic inhibitors of preneyl transferase, preparation and activity of the peptidomimetics, and use for treating tumors', 18 July 1996, PCT Int. Appl 186 pp., see the entire abstract.	1-19

☐ Further documents are listed in the continuation of Box C. ☐ See patent family annex.

*	Special categories of cited documents:	"T"	later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"A"	document defining the general state of the art which is not considered to be of particular relevance	"X"	document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"E"	earlier document published on or after the international filing date	"Y"	document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"L"	document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	"&"	document member of the same patent family
"O"	document referring to an oral disclosure, use, exhibition or other means		
"P"	document published prior to the international filing date but later than the priority date claimed		

Date of the actual completion of the international search 07 SEPTEMBER 1998	Date of mailing of the international search report 16 OCT 1998
Name and mailing address of the ISA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231 Facsimile No. (703) 305-3230	Authorized officer YOGENDRA N. GUPTA Telephone No. (703) 308-1235

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INTERNATIONAL SEARCH REPORT

International application No.
PCT/US98/09296

A. CLASSIFICATION OF SUBJECT MATTER:
IPC (6):

A61K 31/38, 31/39, 31/40, 31/415, 31/42, 31/425, 31/44, 31/445, 31/495, 31/505, 31/095, 31/18; C07D 207/09, 233/54, 239/24, 241/04, 263/02, 277/28, 307/00, 333/00, 209/10;
C07C 303/00, 307/00, 309/00, 311/00, 313/00

A. CLASSIFICATION OF SUBJECT MATTER:
US CL :

514/255, 256, 331, 351, 357, 371, 400, 419, 423, 424, 439, 447, 461, 570, 604; 544/335, 400 ; 546/225, 300, 312, 336; 548/196, 338.1, 495, 543; 549/69, 76, 491; 564/42, 49

B. FIELDS SEARCHED
Minimum documentation searched
Classification System: U.S.

514/255, 256, 331, 351, 357, 371, 400, 419, 423, 424, 439, 447, 461, 570, 604; 544/335, 400 ; 546/225, 300, 312, 336; 548/196, 338.1, 495, 543; 549/69, 76, 491; 564/42, 49